



STIC Search Report

Biotech-Chem Library

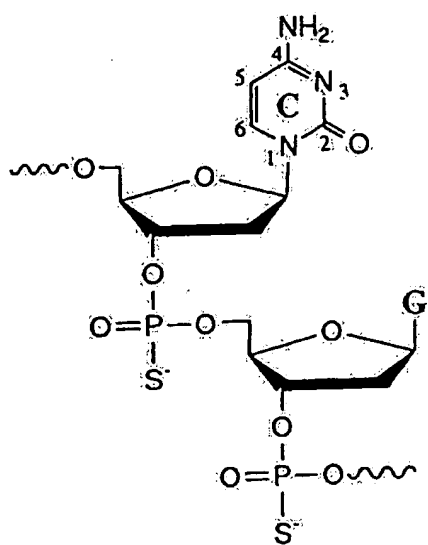
STIC Database Tracking Number: 125834

TO: Emily M Le
Location: 3c35 / 3c18
Tuesday, June 29, 2004
Art Unit: 1648
Phone: 272-0903
Serial Number: 09 / 965116

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes



SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: _____ Examiner #: _____ Date: _____
Art Unit: _____ Phone Number 30 _____ Serial Number: _____
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

=> fil reg

FILE 'REGISTRY' ENTERED AT 06:25:19 ON 29 JUN 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 JUN 2004 HIGHEST RN 700803-86-7

DICTIONARY FILE UPDATES: 28 JUN 2004 HIGHEST RN 700803-86-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

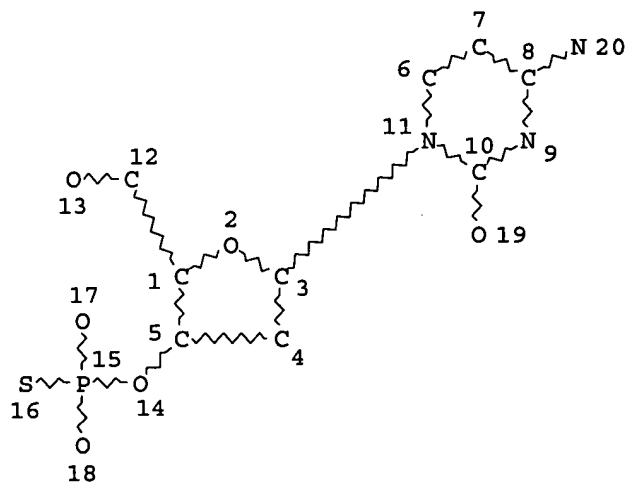
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l25

L15 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

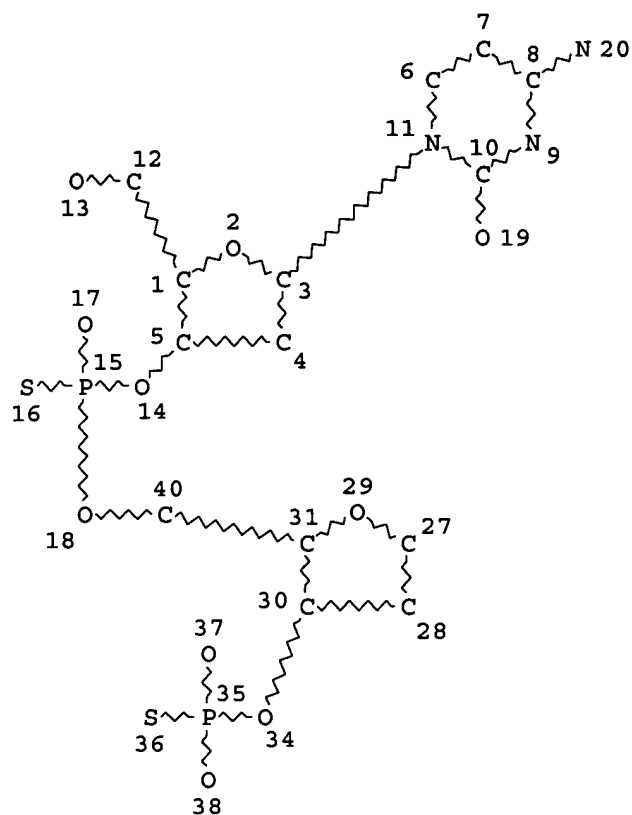
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

L17 1004 SEA FILE=REGISTRY SSS FUL L15

L19 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

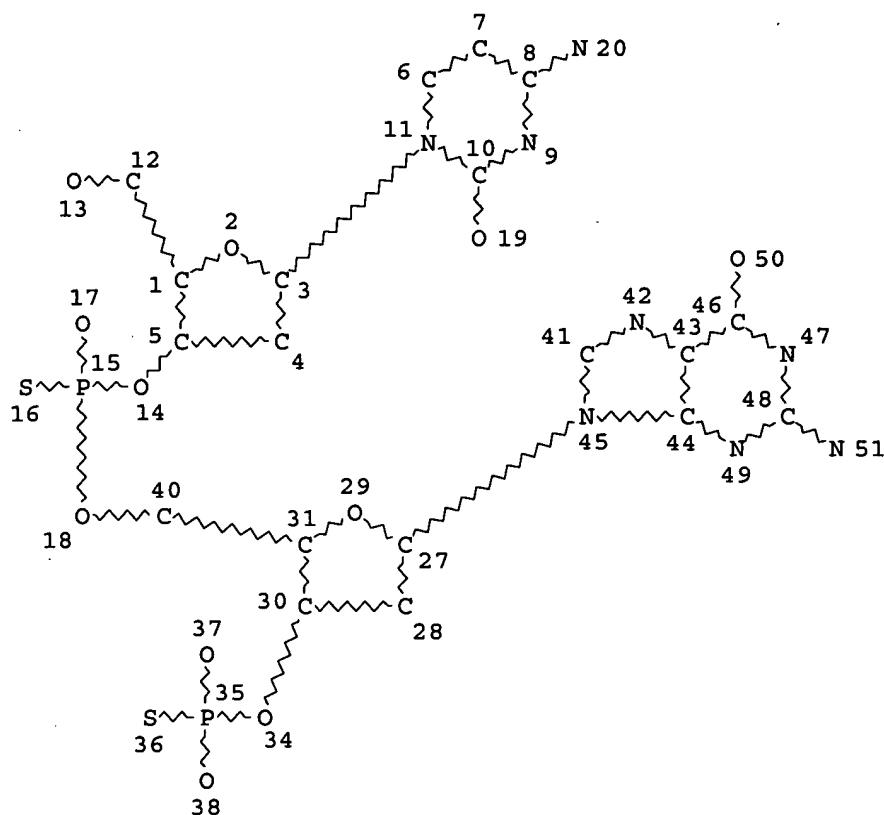
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NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE

L21 520 SEA FILE=REGISTRY SUB=L17 SSS FUL L19

L22 STR



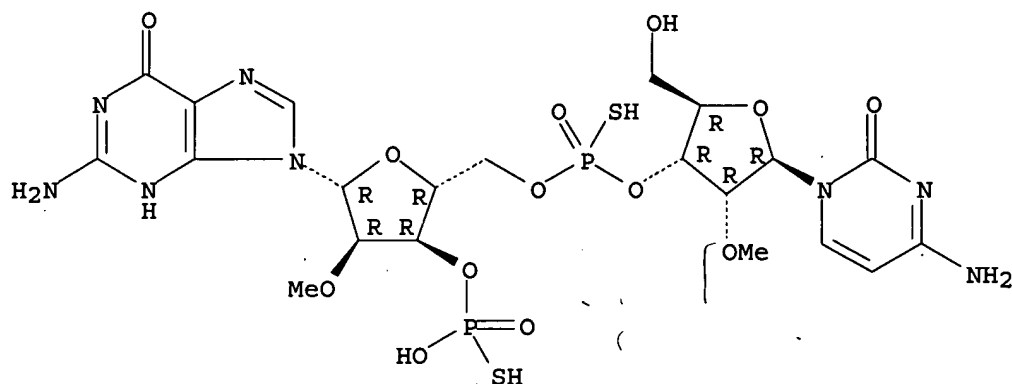
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NUMBER OF NODES IS 42

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L25      4 SEA FILE=REGISTRY ABB=ON PLU=ON L24 AND 5/NR
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L25  ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   352670-02-1  REGISTRY
CN   Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-O-methyl-,
      3'-(dihydrogen phosphorothioate) (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C21 H30 N8 O13 P2 S2
SR   CA
LC   STN Files:  CA, CAPLUS, USPATFULL
DT.CA  Caplus document type:  Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); CMBI (Combinatorial
      study); PREP (Preparation); USES (Uses)
RL.NP  Roles from non-patents:  PREP (Preparation)
```

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:311149

REFERENCE 2: 135:153070

L25 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN

RN 352669-86-4 REGISTRY

CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-O-methyl-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C20 H28 N8 O12 P2 S2

SR CA

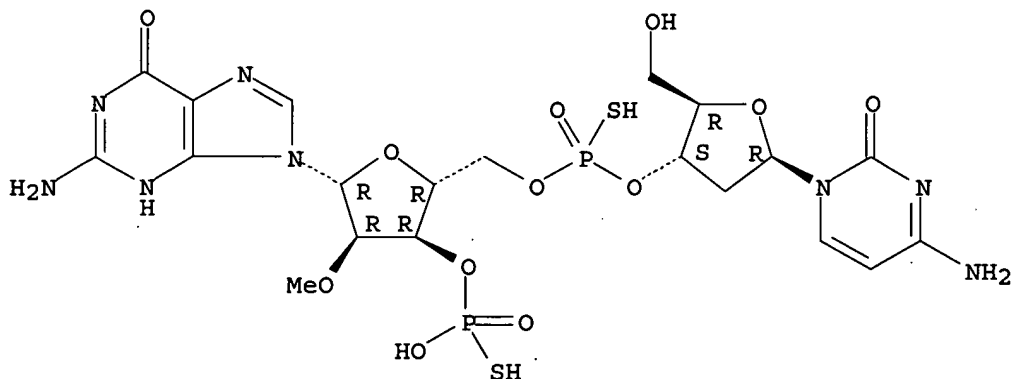
LC STN Files: CA, CAPLUS, USPATFULL

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); CMBI (Combinatorial
study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: PREP (Preparation)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:311149

REFERENCE 2: 135:153070

L25 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN

RN 352669-70-6 REGISTRY

CN Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C20 H28 N8 O12 P2 S2

SR CA

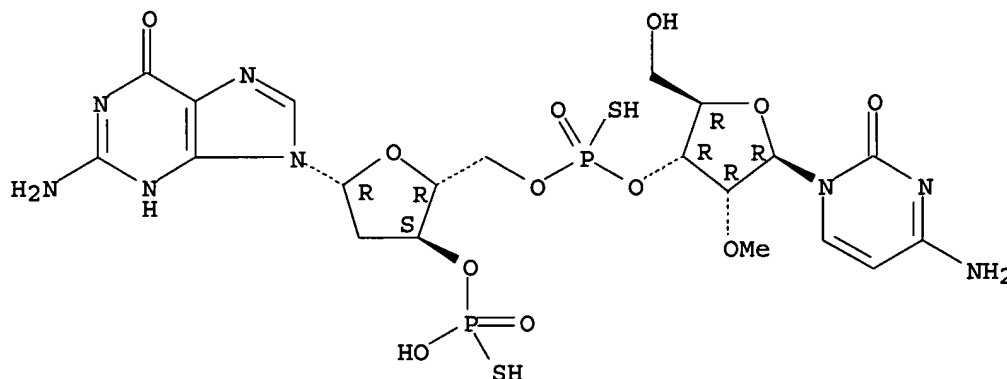
LC STN Files: CA, CAPLUS, USPATFULL

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: PREP (Preparation)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:311149

REFERENCE 2: 135:153070

L25 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN

RN 352669-53-5 REGISTRY

CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME).

FS STEREOSEARCH

MF C19 H26 N8 O11 P2 S2

SR CA

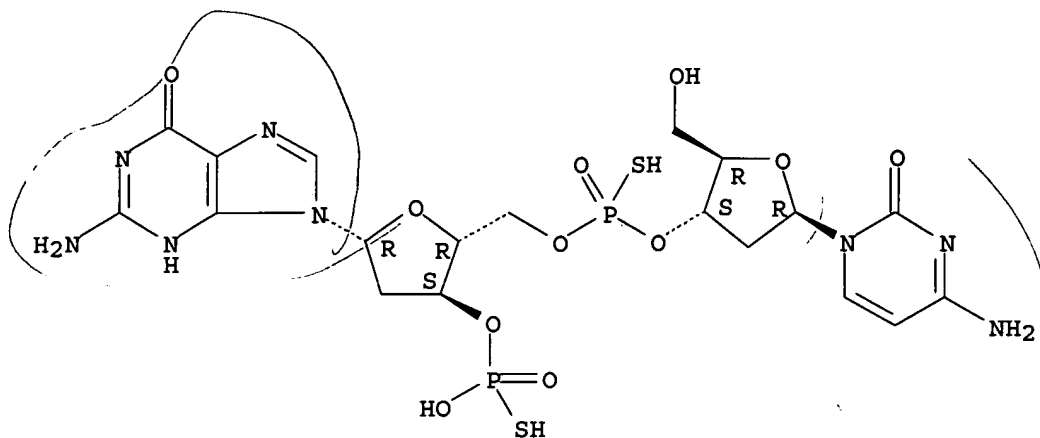
LC STN Files: CA, CAPLUS, USPATFULL

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: PREP (Preparation)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:311149

REFERENCE 2: 135:153070

=> d his

(FILE 'HOME' ENTERED AT 05:54:16 ON 29 JUN 2004)
SET COST OFF

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L1 4 S US20020137714/PN OR (US2000-712898# OR US2000-235453# OR US20
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L2 81 S E4-E9
E AGRAWAL S/AU
L3 388 S E3-E15
E AGRAWAL SUDHIR/AU
L4 355 S E3
E YU D/AU
L5 440 S E3-E30
E YU DONG/AU
L6 449 S E3-E73
E ZHAO Q/AU
L7 417 S E3-E17
E ZHAO QUI/AU
L8 1 S E13
E HYBRIDON/PA,CS
L9 346 S E3-E34
SEL RN L1

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L11 0 S L10 AND (P AND S)/ELS
L12 1 S L10 AND S/ELS
L13 1 S L10 AND P/ELS
L14 2 S L12,L13
L15 STR
L16 50 S L15
L17 1004 S L15 FUL
SAV L17 TEMP LE965/A

L18 STR L15
 L19 STR L18
 L20 27 S L19 SAM SUB=L17
 L21 520 S L19 FUL SUB=L17
 SAV L21 LE965A/A
 L22 STR L19
 L23 13 S L22 SAM SUB=L21
 L24 247 S L22 FUL SUB=L21
 SAV L24 LE965B/A
 L25 4 S L24 AND 5/NR
 L26 1 S L25 AND C19H26N8O11P2S2

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FILE 'USPATFULL, USPAT2' ENTERED AT 06:09:44 ON 29 JUN 2004

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 L29 1 S L25
 L30 1 S L28,L29

FILE 'HCAPLUS' ENTERED AT 06:10:46 ON 29 JUN 2004

L31 2 S L26
 L32 2 S L25
 L33 2 S L31,L32
 L34 56 S L24
 L35 1 S L34 AND L1-L9
 E ZHAO QIU/AU
 L36 4 S E3
 L37 37 S E34
 L38 1 S L34 AND L36,L37
 L39 1 S L35,L38
 L40 3 S L33,L39
 L41 279 S L17
 L42 13 S L41 AND L1-L9,L36,L37
 SEL HIT RN

FILE 'REGISTRY' ENTERED AT 06:14:07 ON 29 JUN 2004

L43 24 S E1-E24

FILE 'HCAPLUS' ENTERED AT 06:17:04 ON 29 JUN 2004

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 L45 0 S L1-L9,L36,L37 AND ?PHOSPHOTHIO?
 L46 259 S L1-L9,L36,L37 AND ?PHOSPH?(L)?THIO?
 L47 256 S L46 AND (?NUCLEO? OR ?NUCLEI?)
 E PHOSPHORTHIOATE/CT
 E PHOSPHOROTHIOATE/CT
 L48 2068 S E5+OLD,NT,PFT OR E6+OLD,NT,PFT OR E7
 E E5+ALL
 L49 948 S E28,E27+NT
 E E26+ALL
 L50 2068 S E10,E9+NT
 L51 112 S L46 AND L48-L50
 L52 112 S L47 AND L51
 L53 112 S L51,L52
 L54 99 S L53 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
 L55 112 S L53,L54 AND L48-L50
 L56 115 S L1,L55
 L57 126 S L42,L56
 L58 125 S L57 NOT L40

FILE 'REGISTRY' ENTERED AT 06:25:19 ON 29 JUN 2004

=> fil uspatall

FILE 'USPATFULL' ENTERED AT 06:25:34 ON 29 JUN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 06:25:34 ON 29 JUN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d l30 bib abs hitstr tot

L30 ANSWER 1 OF 1 USPATFULL on STN
AN 2003:127044 USPATFULL
TI Thiophosphate nucleic acid-based compounds
IN Iyer, Radhakrishnan P., Shrewsbury, MA, UNITED STATES
PA Micrologix Biotech Inc., Vancouver, CANADA (U.S. corporation)
PI US 2003087256 A1 20030508
AI US 2002-118480 A1 20020408 (10)
PRAI US 2001-282098P 20010406 (60)
DT Utility
FS APPLICATION
LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300,
SEATTLE, WA, 98104-7092
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 624
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention comprises short, thiophosphate nucleic acids (primarily mono-, di-, and tri-nucleotides), libraries comprising them, and methods of using them as therapeutic anti-viral (particularly anti-HBV) agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

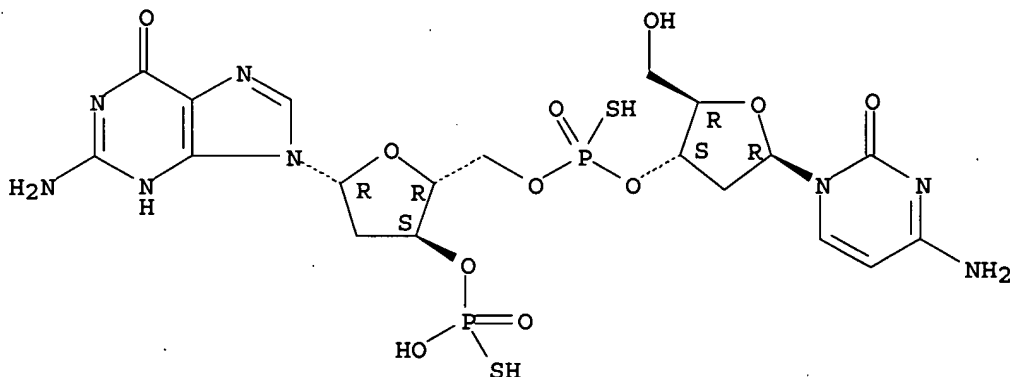
IT 352669-53-5P 352669-70-6P 352669-86-4P
352670-02-1P

(solid phase synthesis and combinatorial library of thiophosphate nucleic acids as antiviral agents)

RN 352669-53-5 USPATFULL

CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

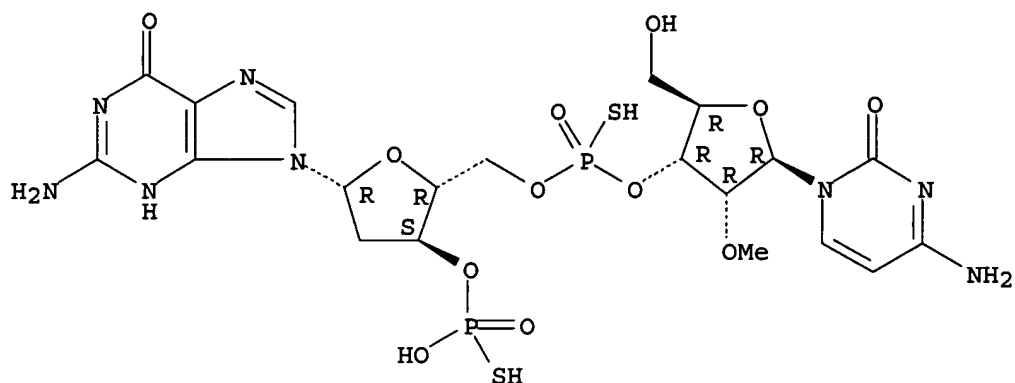
Absolute stereochemistry.



RN 352669-70-6 USPATFULL

CN Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

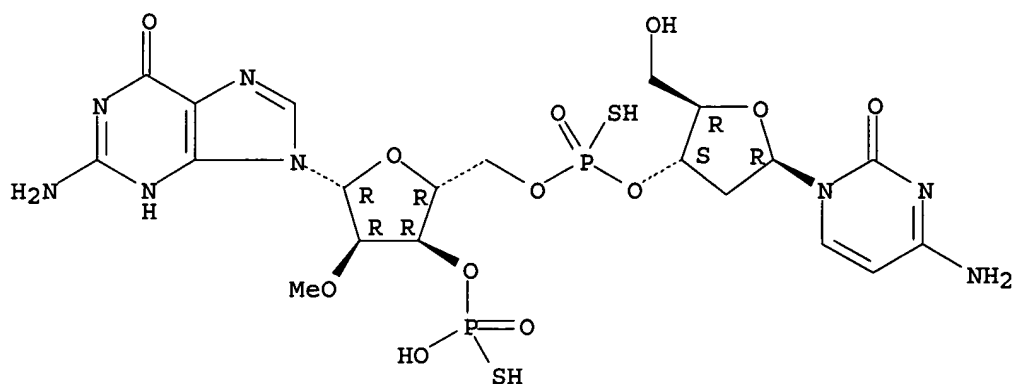
Absolute stereochemistry.



RN 352669-86-4 USPATFULL

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3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

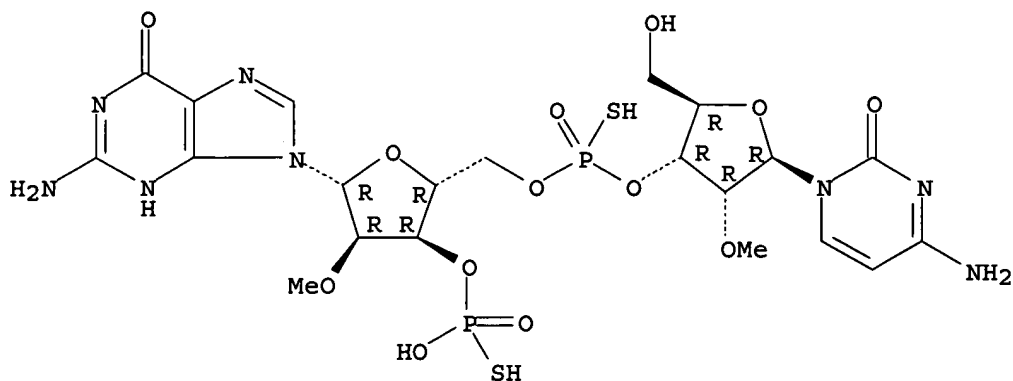
Absolute stereochemistry.



RN 352670-02-1 USPATFULL

CN Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-O-methyl-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> fil hcaplus
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 29 Jun 2004 VOL 141 ISS 1
 FILE LAST UPDATED: 28 Jun 2004 (20040628/ED)

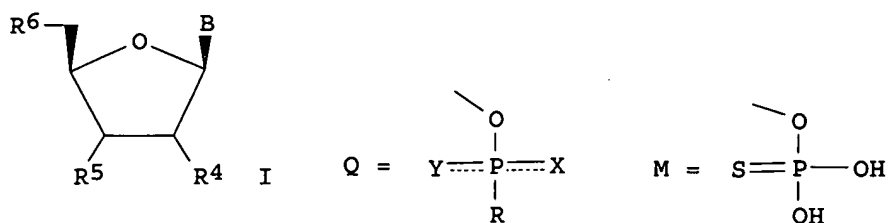
This file contains CAS Registry Numbers for easy and accurate substance identification.

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L40 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:793628 HCAPLUS
 DN 137:311149
 ED Entered STN: 18 Oct 2002
 TI Solid phase synthesis and combinatorial library of thiophosphate nucleic acids as antiviral agents
 IN Iyer, Radhakrishnan P.
 PA Origenix Technologies, Inc., Can.
 SO PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D487-04
 ICS C07D405-04
 CC 33-9 (Carbohydrates)
 Section cross-reference(s): 1, 63

FAN.CNT 1

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PI	WO 2002081476	A1	20021017	WO 2002-US10897	20020408
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	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003087256	A1	20030508	US 2002-118480	20020408
PRAI	US 2001-282098P	P	20010406		
OS	MARPAT 137:311149				
GI					



- AB The invention comprises combinatorial library solid phase synthesis of thiophosphate nucleic acids (primarily mono-, di-, and tri-nucleotides) I, wherein R4 is R3 or OR3; one of R5 and R6 is Q or M; X and Y are independently O, S, Se, NR1, NR1NR2 CR1CR2, OR7, SR7, SeR7, provided at least one of X and Y is S; R is -OH, a mononucleoside, or dinucleotide; R1, R2, R3, and R7 are independently H or a C1-C20 hydrophobic moiety; and B is a purine or pyrimidine base, and methods of using them as therapeutic anti-viral (particularly anti-HBV) agents (no antiviral data). Thus, a sixty-four member library representing thiophosphate 3'-psWZ dimer sequences (W,Z = dA, dC, dG, dT, 2'-OMe-rA, 2'-OMe-rC, 2'-OMe-rG or 2'-OMe-rU) was prepared in 50 to 55 % yield using this approach.
- ST antiviral hepatitis combinatorial library synthesis thiophosphate oligonucleotide human; combinatorial library solid phase synthesis thiophosphate nucleic acid oligonucleotide
- IT Antiviral agents
(solid phase synthesis and combinatorial library of thiophosphate nucleic acids as anti-HBV antiviral agents)
- IT Combinatorial library
Hepatitis B virus
Human
Solid phase synthesis
(solid phase synthesis and combinatorial library of thiophosphate nucleic acids as antiviral agents)
- IT Nucleic acids
Oligonucleotides
RL: CPN (Combinatorial preparation); IMF (Industrial manufacture); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(thiophosphates; solid phase synthesis and combinatorial library of thiophosphate nucleic acids as antiviral agents)
- IT Infection
(viral; solid phase synthesis and combinatorial library of thiophosphate nucleic acids as antiviral agents)
- IT 273933-35-0P 470692-27-4DP, CPG polymer support
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(solid phase synthesis and combinatorial library of thiophosphate nucleic acids as antiviral agents)
- IT 352669-44-4P 352669-45-5P 352669-46-6P 352669-47-7P 352669-48-8P
352669-49-9P 352669-50-2P 352669-51-3P 352669-52-4P
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352669-63-7P 352669-64-8P 352669-65-9P 352669-66-0P 352669-67-1P
352669-68-2P 352669-69-3P **352669-70-6P** 352669-71-7P
352669-72-8P 352669-73-9P 352669-74-0P 352669-75-1P 352669-76-2P
352669-77-3P 352669-78-4P 352669-79-5P 352669-80-8P 352669-81-9P
352669-82-0P 352669-83-1P 352669-84-2P 352669-85-3P
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352670-00-9P 352670-01-0P **352670-02-1P** 352670-03-2P
 352670-04-3P 352670-05-4P 352670-06-5P 352670-07-6P 352670-08-7P
 RL: CPN (Combinatorial preparation); IMF (Industrial manufacture); PAC
 (Pharmacological activity); THU (Therapeutic use); BIOL (Biological
 study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
 (solid phase synthesis and combinatorial library of thiophosphate
 nucleic acids as antiviral agents)

IT 87-86-5, Pentachlorophenol 107-10-8D, 1-Propanamine, CPG polymer support
 108-30-5, Succinic anhydride, reactions 623-05-2, 4-Hydroxybenzyl
 alcohol 25952-53-8
 RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial
 study); RACT (Reactant or reagent)
 (solid phase synthesis and combinatorial library of thiophosphate
 nucleic acids as antiviral agents)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Letsinger; US 4958013 A 1990 HCAPLUS

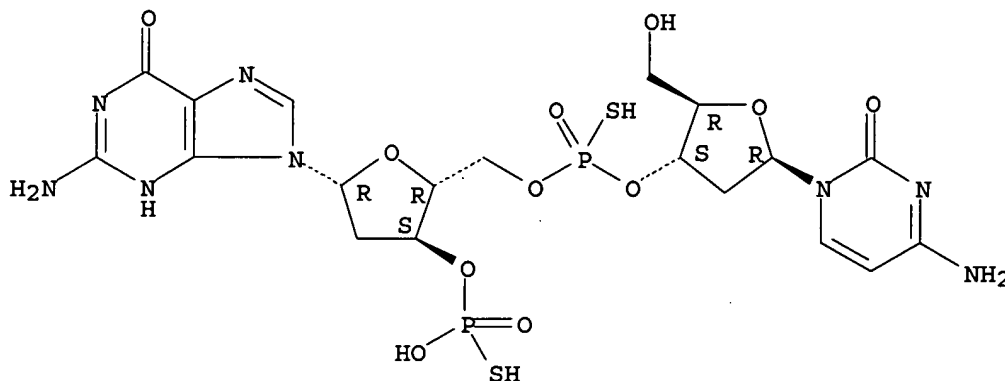
IT **352669-53-5P 352669-70-6P 352669-86-4P**
352670-02-1P

RL: CPN (Combinatorial preparation); IMF (Industrial manufacture); PAC
 (Pharmacological activity); THU (Therapeutic use); BIOL (Biological
 study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
 (solid phase synthesis and combinatorial library of thiophosphate
 nucleic acids as antiviral agents)

RN 352669-53-5 HCAPLUS

CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-,
 3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

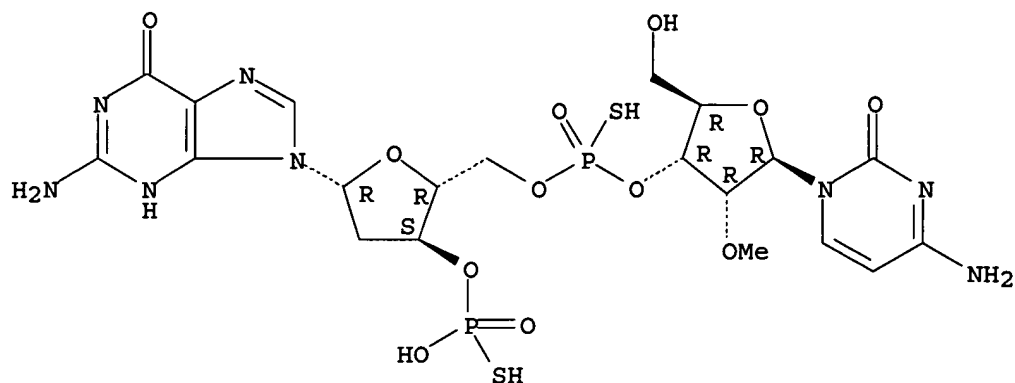
Absolute stereochemistry.



RN 352669-70-6 HCAPLUS

CN Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-deoxy-,
 3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

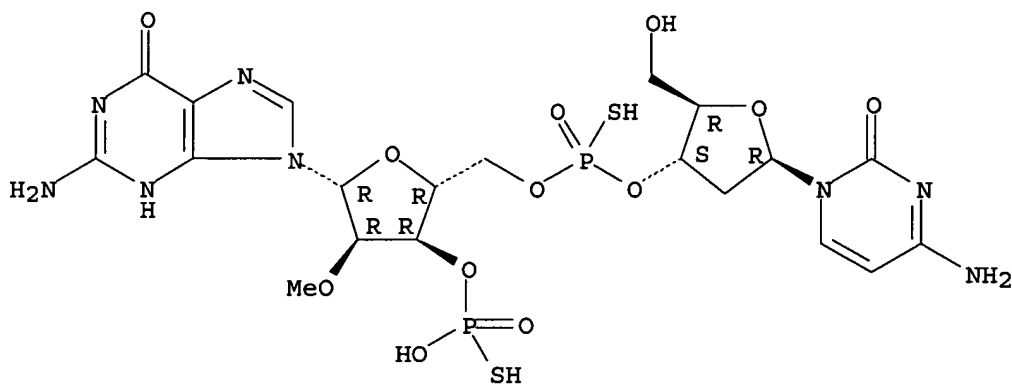
Absolute stereochemistry.



RN 352669-86-4 HCAPLUS

CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-O-methyl-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

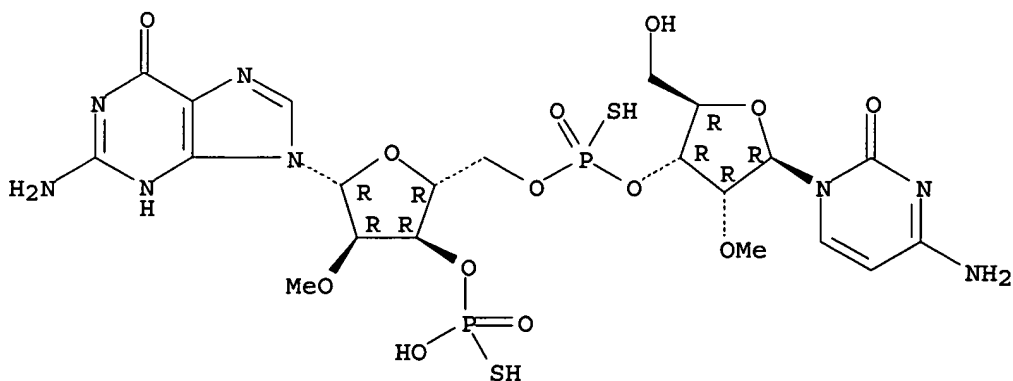
Absolute stereochemistry.



RN 352670-02-1 HCAPLUS

CN Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-O-methyl-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 2001:372445 HCAPLUS
 DN 135:153070
 ED Entered STN: 24 May 2001
 TI A novel linker for the solid-phase synthesis of a library of
 3'-thiophosphorylated dinucleotides
 AU Roland, Arlene; Xiao, Yufang; Jin, Yi; Iyer, Radhakrishnan P.
 CS Origenix Technologies Inc., Laval, QC, H7V 4A9, Can.
 SO Tetrahedron Letters (2001), 42(22), 3669-3672
 CODEN: TELEAY; ISSN: 0040-4039
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 CC 33-10 (Carbohydrates)
 Section cross-reference(s): 9
 OS CASREACT 135:153070
 AB The preparation of a controlled-pore-glass (CPG) support carrying a novel
 linker [DMT-O-CH₂-4-C₆H₄ O-C(O)(CH₂)₂C(O)-] (DMT = 4,4'-dimethoxytrityl)
 is described. The supported linker was prepared by succinylating the amine
 group of amino-alkyl CPG, followed by reaction with HO-4-C₆H₄CH₂O-DMT.
 This support was compatible with the established phosphoramidite method of
 solid-phase oligonucleotide synthesis. The use of this linker for the
 synthesis of a library of 3'-thiophosphorylated dinucleotides is
 described.
 ST CPG support linker solid phase prepn thiophosphoryl oligonucleotide
 library
 IT Combinatorial library
 Solid phase synthesis
 (preparation of 3'-thiophosphorylated dinucleotides using CPG-linker
 solid-phase methods)
 IT Oligonucleotides
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of 3'-thiophosphorylated dinucleotides using CPG-linker
 solid-phase methods)
 IT 87-86-5, Pentachlorophenol
 RL: RGT (Reagent); RACT (Reactant or reagent)
 (preparation of)
 IT 108-30-5, Succinic anhydride, reactions 623-05-2, 4-
 (Hydroxymethyl)phenol
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of 3'-thiophosphorylated dinucleotides using CPG-linker
 solid-phase methods)
 IT 110-15-6DP, Succinic acid, aminoalkyl CPG-bound, preparation
 273933-35-0P 352669-43-3DP, aminoalkyl CPG-bound
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of 3'-thiophosphorylated dinucleotides using CPG-linker
 solid-phase methods)
 IT 352669-44-4P 352669-45-5P 352669-46-6P 352669-47-7P 352669-48-8P
 352669-49-9P 352669-50-2P 352669-51-3P 352669-52-4P
352669-53-5P 352669-54-6P 352669-55-7P 352669-56-8P
 352669-57-9P 352669-58-0P 352669-59-1P 352669-60-4P 352669-62-6P
 352669-63-7P 352669-64-8P 352669-65-9P 352669-66-0P 352669-67-1P
 352669-68-2P 352669-69-3P **352669-70-6P** 352669-71-7P
 352669-72-8P 352669-73-9P 352669-74-0P 352669-75-1P 352669-76-2P
 352669-77-3P 352669-78-4P 352669-79-5P 352669-80-8P 352669-81-9P
 352669-82-0P 352669-83-1P 352669-84-2P 352669-85-3P
352669-86-4P 352669-87-5P 352669-88-6P 352669-89-7P
 352669-90-0P 352669-91-1P 352669-92-2P 352669-93-3P 352669-94-4P
 352669-95-5P 352669-96-6P 352669-97-7P 352669-98-8P 352669-99-9P
 352670-00-9P 352670-01-0P **352670-02-1P** 352670-03-2P
 352670-04-3P 352670-05-4P 352670-06-5P 352670-07-6P 352670-08-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of 3'-thiophosphorylated dinucleotides using CPG-linker

solid-phase methods)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Asseline, U; Tetrahedron 1992, V48, P1233 HCAPLUS
- (2) Asseline, U; Tetrahedron Lett 1989, V30, P2521 HCAPLUS
- (3) Beaucage, S; Tetrahedron 1992, V48, P2223 HCAPLUS
- (4) Beaucage, S; Tetrahedron 1993, V49, P1925 HCAPLUS
- (5) Beaucage, S; Tetrahedron Lett 1981, V22, P1859 HCAPLUS
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- (7) Dolinnaya, N; Nucleic Acids Res 1993, V21, P5403 HCAPLUS
- (8) Felder, E; Tetrahedron Lett 1984, V25, P3967 HCAPLUS
- (9) Gryaznov, S; Tetrahedron Lett 1992, V33, P4127 HCAPLUS
- (10) Guzaev, A; Tetrahedron Lett 1997, V38, P3989 HCAPLUS
- (11) Iyer, R; Bioorg Chem Lett 1996, V6, P1917 HCAPLUS
- (12) Iyer, R; J Am Chem Soc 1990, V112, P1253 HCAPLUS
- (13) Jin, Y; Bioorg Med Chem Lett 2000, V10, P1921 HCAPLUS
- (14) Kumar, P; Chem Lett 1997, P1231 HCAPLUS
- (15) Kumar, P; Tetrahedron Lett 1991, V32, P967 HCAPLUS
- (16) Markiewicz, W; Nucleic Acids Res 1989, V17, P7149 HCAPLUS
- (17) McMinn, D; Tetrahedron Lett 1998, V39, P4155 HCAPLUS
- (18) Prakash, G; J Am Chem Soc 1992, V114, P3523 HCAPLUS
- (19) Wang, S; Nucleic Acids Res 1994, V22, P2326 HCAPLUS

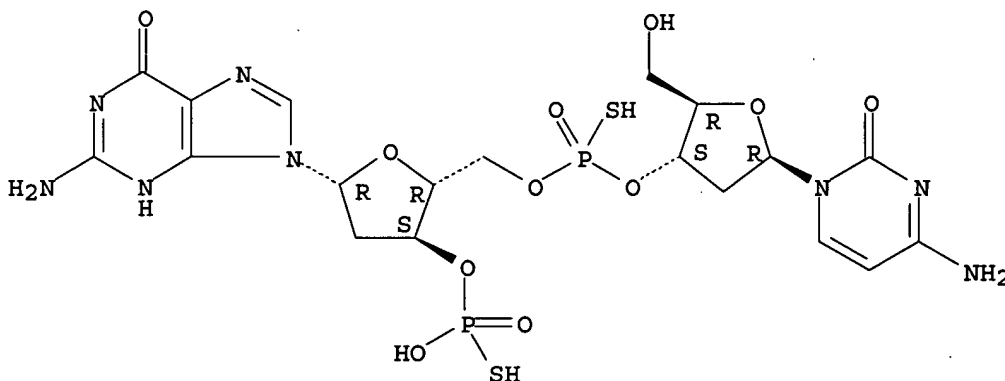
IT 352669-53-5P 352669-70-6P 352669-86-4P
352670-02-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 3'-thiophosphorylated dinucleotides using CPG-linker
solid-phase methods)

RN 352669-53-5 HCAPLUS

CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 352669-70-6 HCAPLUS

CN Guanosine, 2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-deoxy-,
3'-(dihydrogen phosphorothioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

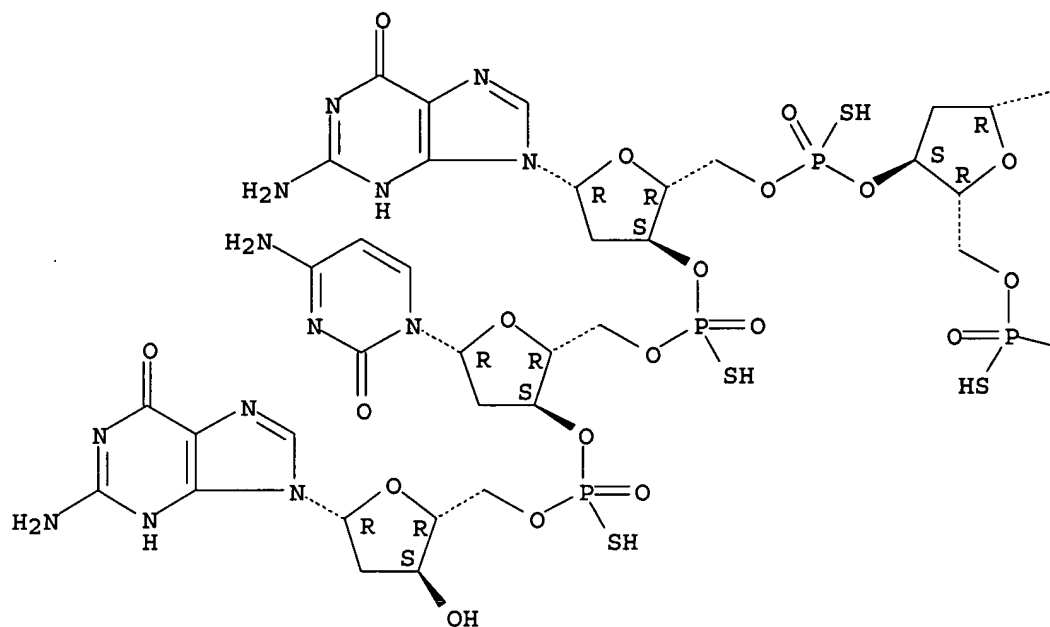
AN 1996:51749 HCAPLUS
 DN 124:193281
 ED Entered STN: 25 Jan 1996
 TI Effect of different chemically modified oligodeoxynucleotides on immune stimulation
 AU Zhao, Qiuyan; Tamsamani, Jamal; Iadarola, Patricia L.; Jiang, Zhiwei; Agrawal, Sudhir
 CS Hybridon Inc., Worcester, MA, 01605, USA
 SO Biochemical Pharmacology (1996), 51(2), 173-82
 CODEN: BCPA6; ISSN: 0006-2952
 PB Elsevier
 DT Journal
 LA English
 CC 1-3 (Pharmacology)
 AB Based on previous studies that certain oligonucleotides can stimulate cell proliferation and Ig production, this study was carried out to establish the relationship between the stimulatory effect and the chemical modification of the oligonucleotide. First, the effects of oligonucleotide and analogs on immune stimulation were studied in vitro using murine splenic lymphocytes. Our results show that cell proliferation and Ig production (IgG and IgM) depend on the sequence and the chemical modification of the oligonucleotide. Phosphorothioate oligodeoxynucleotides displayed a greater stimulatory effect than partially modified phosphorothioate oligonucleotides. Second, we studied the effects of these chemical modified oligonucleotides after injection in mice. Massive splenomegaly and stimulation of cell proliferation were observed with some phosphorothioate oligonucleotides. These effects were minimized markedly by chimeric and hybrid oligonucleotides. We also demonstrate that in vitro the effects of oligonucleotides on murine lymphocytes were unaffected by T cell depletion, suggesting that oligonucleotides exert their effects mainly on the B cells.
 ST oligodeoxynucleotide immunostimulant B cell structure
 IT Immunostimulants
 Molecular structure-biological activity relationship
 (effect of different chemical modified oligodeoxynucleotides on immune stimulation)
 IT Lymphocyte
 (B-cell, in effect of different chemical modified oligodeoxynucleotides on immune stimulation)
 IT Nucleotides, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (oligo-, deoxyribo-, effect of different chemical modified oligodeoxynucleotides on immune stimulation)
 IT 148711-35-7P 151219-07-7P 151285-76-6P 153021-75-1P 160740-60-3P
 160740-62-5P 174207-92-2P 174207-93-3P 174207-94-4P 174207-95-5P
 174207-96-6P 174207-97-7P 174207-98-8P 174207-99-9P 174208-00-5P
 174208-01-6P 176369-99-6P 176836-36-5P 176836-37-6P
 176836-38-7P 176836-39-8P 176836-40-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (effect of different chemical modified oligodeoxynucleotides on immune stimulation)
 IT 176369-99-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (effect of different chemical modified oligodeoxynucleotides on immune stimulation)

RN 176369-99-6 HCAPLUS

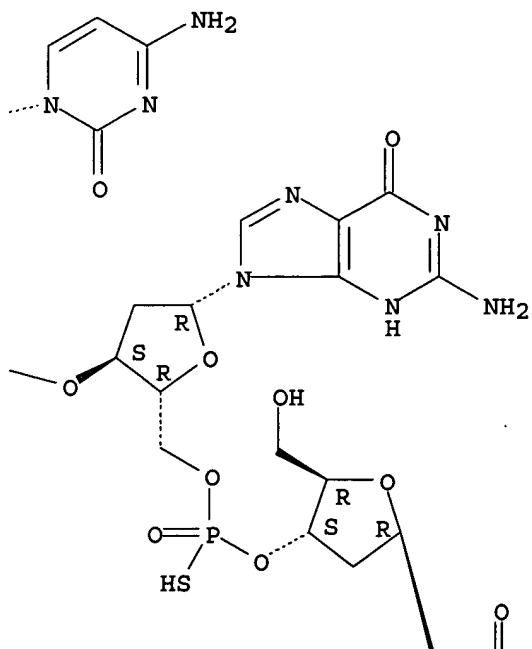
CN Guanosine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-P-thioguananylyl-(3'→5')-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-P-thioguananylyl-(3'→5')-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

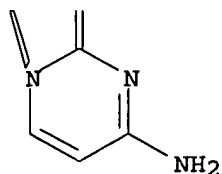
PAGE 1-A



PAGE 1-B



PAGE 2-B



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L58 ANSWER 1 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:414675 HCAPLUS

DN 140:405475

TI Modulation of immunostimulatory properties of **oligonucleotide**-based compounds by optimal presentation of 5' endsIN **Agrawal, Sudhir; Kandimalla, Ekambar R.; Yu, Dong; Bhagat, Lakshmi**PA **Hybridon, Inc., USA**

SO U.S. Pat. Appl. Publ., 67 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004097719	A1	20040520	US 2002-279684	20021024
PRAI	US 2002-279684		20021024		

AB The authors disclose the therapeutic use of **oligonucleotides** as immunostimulatory agents in immunotherapy applications. More particularly, the invention provides linear and branched **oligonucleotides** joined by their 3'-terminus (immunomers) for generating an immune response or for treating a patient in need of immunostimulation. The immunomers of the invention comprise at least two **oligonucleotides** linked at their 3' ends, **internucleoside** linkages or functionalized **nucleobase** or sugar to a non-**nucleotidic** linker, at least one of the **oligonucleotides** being an immunostimulatory **oligonucleotide** and having an accessible 5' end.

L58 ANSWER 2 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:304228 HCAPLUS

DN 140:418706

TI Hybridization-based fluorescence assay allows quantitation of single-stranded **oligodeoxynucleotides** in low nanomolar rangeAU **Kandimalla, Ekambar R.; Pandey, Rajendra K.; Agrawal, Sudhir**CS **Hybridon, Inc., Cambridge, MA, 02139, USA**

SO Analytical Biochemistry (2004), 328(1), 93-95

CODEN: ANBCA2; ISSN: 0003-2697

PB Elsevier Science

DT Journal

LA English

AB The study presents a hybridization-based fluorescence assay for determining concns. of single-stranded (ss) **oligonucleotides** in solution. Two fluorophores ethidium bromide and Hoechst 33258, which bind to dsDNA but not ssDNA, were used. By adding these fluorophores and a complementary **oligonucleotide** to form a duplex, **oligonucleotides** of

interest can be quantitated. The assay is sensitive and reproducible down to 0.6µg/mL of a 20-mer ss **oligonucleotide**. The method also worked equally well with **phosphorothioate oligonucleotides** that are used most commonly in antisense applications.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 3 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:178004 HCAPLUS

DN 140:247049

TI Modulation of immunostimulatory properties of **oligonucleotide**-based compounds by optimal presentation of 5'ends

IN **Agrawal, Sudhir; Kandimalla, Ekambar; Yu, Dong**
; Bhagat, Lakshmi

PA **Hybridon, Inc., USA**

SO Eur. Pat. Appl., 93 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1393745	A1	20040303	EP 2003-17211	20030729
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-399181P	P	20020729		
	US 2002-399287P	P	20020729		
	US 2002-399302P	P	20020729		
	US 2002-399343P	P	20020729		
	US 2002-399344P	P	20020729		
OS	MARPAT 140:247049				
AB	The invention relates to the therapeutic use of oligonucleotides as immunostimulatory agents in immunotherapy applications. More particularly, the invention provides immunomers for use in methods for generating an immune response or for treating a patient in need of immunostimulation. The immunomers of the invention comprise at least two oligonucleotides linked at their 3' ends, internucleoside linkages or functionalized nucleobase or sugar to a non- nucleotidic linker, at least one of the oligonucleotides being an immunostimulatory oligonucleotide and having an accessible 5' end.				

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 4 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:1007843 HCAPLUS

DN 140:35939

TI Modulation of oligonucleotide CpG-mediated immune stimulation by positional modification of nucleosides

IN **Agrawal, Sudhir; Kandimalla, Ekambar R.**

PA USA

SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Pat. Appl. 2002 132,995.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003236211	A1	20031225	US 2003-406015	20030403
	US 2002132995	A1	20020919	US 2001-845623	20010430 <--
	US 2003212029	A1	20031113	US 2003-365834	20030213

PRAI US 2001-845623 A2 20010430
US 2000-201578P P 20000501 <--

OS MARPAT 140:35939

AB The invention provides methods for modulating the immune response caused by CpG dinucleotide-containing compds. The methods according to the invention enables both decreasing the immunostimulatory effect for antisense applications, as well as increasing the immunostimulatory effect for immunotherapy applications.

L58 ANSWER 5 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:991151 HCAPLUS

DN 140:47510

TI Sensitization of cells to cytotoxic agents using **oligonucleotides** directed to **nucleotide** excision repair or transcription-coupled repair genes

IN **Agrawal, Sudhir; Kandimalla, Ekambar R.**; Bregman, David B.; Mani, Sridhar; Lu, Yi

PA USA

SO U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003232767	A1	20031218	US 2001-825489	20010403
PRAI	US 2001-825489		20010403		

AB This invention relates to the fields of mol. biol. and oncol. More particularly, this invention relates to the sensitization of cancerous cells to therapeutic agents. The invention provides methods, compns., and formulations for potentiating or enhancing the toxicity of various cytotoxins and oxidizing agents, and of reducing the resistance and proliferation rate of cancer cells. It also provides various compns. and therapeutic formulations useful as anticancer agents.

L58 ANSWER 6 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:955196 HCAPLUS

DN 140:157045

TI A **dinucleotide** motif in **oligonucleotides** shows potent immunomodulatory activity and overrides species-specific recognition observed with CpG motif

AU **Kandimalla, Ekambar R.**; Bhagat, Lakshmi; Zhu, Fu-gang; Yu, Dong; Cong, Yan-ping; Wang, Daqing; Tang, Jimmy X.; Tang, Jin-yan; Knetter, Cathrine F.; Lien, Egil; **Agrawal, Sudhir**

CS **Hybridon, Inc., Cambridge, MA, 02139, USA**

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(24), 14303-14308
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Bacterial and synthetic DNAs containing CpG **dinucleotides** in specific sequence contexts activate the vertebrate immune system through Toll-like receptor 9 (TLR9). In the present study, we used a synthetic **nucleoside** with a bicyclic heterobase [1-(2'-deoxy- β -D-ribofuranosyl)-2-oxo-7-deaza-8-methyl-purine; R] to replace the C in CpG, resulting in an RpG **dinucleotide**. The RpG **dinucleotide** was incorporated in mouse- and human-specific motifs in **oligodeoxynucleotides** (oligos) and 3'-3-linked oligos, referred to as immunomers. Oligos containing the RpG motif induced cytokine secretion in mouse spleen-cell cultures. Immunomers containing RpG **dinucleotides** showed activity in transfected-HEK293 cells stably expressing mouse TLR9, suggesting direct involvement of TLR9 in the recognition of RpG motif. In

J774 macrophages, RpG motifs activated NF- κ B and mitogen-activated protein kinase pathways. Immunomers containing the RpG **dinucleotide** induced high levels of IL-12 and IFN- γ , but lower IL-6 in time- and concentration-dependent fashion in mouse spleen-cell cultures costimulated with IL-2. Importantly, immunomers containing GTRGTT and GARGTT motifs were recognized to a similar extent by both mouse and human immune systems. Addnl., both mouse- and human-specific RpG immunomers potently stimulated proliferation of peripheral blood mononuclear cells obtained from diverse vertebrate species, including monkey, pig, horse, sheep, goat, rat, and chicken. An immunomer containing GTRGTT motif prevented conalbumin-induced and ragweed allergen-induced allergic inflammation in mice. We show that a synthetic bicyclic **nucleotide** is recognized in the C position of a CpG **dinucleotide** by immune cells from diverse vertebrate species without bias for flanking sequences, suggesting a divergent **nucleotide** motif recognition pattern of TLR9.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 7 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:903252 HCAPLUS
DN 139:391335
TI Modified VEGF **oligonucleotides** for inhibition of tumor growth
IN Smyth, Adrienne P.; Robinson, Gregory S.
PA Hybridon, Inc., USA
SO U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 629,730, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6649596	B1	20031118	US 1998-124304	19980729 <--
	US 5641756	A	19970624	US 1995-569926	19951208 <--
	US 6399586	B1	20020604	US 1999-320911	19990527 <--
PRAI	US 1995-569926	A2	19951208	<--	
	US 1996-629730	B2	19960409	<--	
	US 1993-98942	A2	19930727	<--	
	US 1995-378860	A2	19950126	<--	
	US 1995-398945	A2	19950302	<--	
	US 1996-761708	A1	19961206	<--	
	US 1998-124304	B1	19980729	<--	

AB Disclosed are **oligonucleotides** complementary to VEGF-specific **nucleic acid** useful in reducing the expression of VEGF. Also disclosed are pharmaceutical formulations containing such **oligonucleotides** useful for treating various disorders associated with neovascularization and angiogenesis, e.g. cancer.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 8 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:532234 HCAPLUS
DN 139:224423
TI Immunostimulatory activity of CpG **oligonucleotides** containing nonionic methylphosphonate linkages
IN Yu, Dong; Kandimalla, Ekambar B.; Zhao, Qiuyan
; Agrawal, Sudhir
PA USA
SO U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 PI US 2003129605 A1 20030710 US 2002-137687 20020812
 PRAI US 2001-288917P P 20010504

AB Bacterial DNA and synthetic **oligodeoxynucleotides** containing unmethylated CpG motifs in a particular sequence context activate vertebrate immune cells. We examined the significance of neg. charged **internucleoside** linkages in the flanking sequences 5' and 3' to the CpG motif on immunostimulatory activity. Cell proliferation and secretion of IL-12 and IL-6 in mouse spleen cell cultures, and spleen wts. of mice increased significantly when a nonionic linkage was placed at least four or more **internucleoside** linkages away from the CpG motif in the 5'-flanking sequence. When the nonionic linkage was placed closer than three **internucleoside** linkages in the 5'-flanking sequence to the CpG motif, immunostimulatory activity was suppressed compared with that observed with the unmodified parent oligo. In general, the placement of nonionic linkage in the 3'-flanking sequence to the CpG motif either did not affect or slightly increased immunostimulatory activity compared with the parent oligo. These results have significance in understanding CpG **oligonucleotide**-receptor interactions and the development of potent immunomodulatory agents.

L58 ANSWER 9 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:435305 HCAPLUS

DN 139:30778

TI Modified protein kinase A-specific **oligonucleotides** and methods of their use by down-regulation of protein kinase A subunit RI alpha in cancer treatment

IN Agrawal, Sudhir

PA USA

SO U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Provisional Ser. No. 103,098.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003105035	A1	20030605	US 1999-412947	19991005 <--
PRAI	US 1998-103098P	P	19981005	<--	

AB Disclosed are synthetic, modified **oligonucleotides** complementary to, and capable of down-regulating the expression of, **nucleic acid** encoding protein kinase A subunit RI. The modified **oligonucleotides** have from about 15 to about 30 **nucleotides** and are hybrid, inverted hybrid, or inverted chimeric **oligonucleotides**. Also disclosed are therapeutic compns. containing such **oligonucleotides** and methods of using the same. In addition, therapeutic compns. and methods of their use are described which are directed to a synergistic effect resulting from the combination of **oligonucleotides** of the invention and other therapeutic compns. and methods.

L58 ANSWER 10 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:413961 HCAPLUS

DN 139:903

TI Cooperative antisense **oligonucleotides** forming stable complex for AIDS therapy

IN Kandimalla, Ekambar R.; Agrawal, Sudhir

PA USA

SO U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. 6,372,427.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003099959	A1	20030529	US 2002-54429	20020122 <--
	US 6372427	B1	20020416	US 1995-420672	19950412 <--
	WO 2003062472	A1	20030731	WO 2003-US1814	20030122
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1995-420672	A2	19950412 <--		
	US 2002-54429	A	20020122		
AB	Disclosed is a composition comprising at least two synthetic, cooperative oligonucleotides , each comprising a region complementary to one of tandem, non-overlapping regions of a target single-stranded nucleic acid , and each further comprising a non- nucleotidic binding partner at a terminus of each of the oligonucleotides , such that the binding partners can interact with each other to form a stable complex. The binding partners could be cyclodextrin, adamantane, streptavidin or biotin. Also disclosed are dimeric structures, ternary complexes, pharmaceutical formulations, and methods utilizing the cooperative oligonucleotides for AIDS therapy. The target sequence is an mRNA, single-stranded viral RNA and single-stranded viral DNA. The antisense oligonucleotides can target HIV DNA and/or HIV/RNA.				
L58	ANSWER 11 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STM				
AN	2003:261944 HCAPLUS				
DN	138:265633				
TI	Antisense oligonucleotides and methods to induce tumor cell death				
IN	Kandimalla, Ekambar M.; Agrawal, Sudhir; Shankar, Sai Latha; Shafit-Zagardo, Bridget; Mani, Sridhar				
PA	Hybridon, Inc., USA				
SO	PCT Int. Appl., 84 pp. CODEN: PIXXD2				
DT	Patent				
LA	English				
FAN	CNT 1				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003027244	A2	20030403	WO 2002-US30276	20020924
	WO 2003027244	A3	20031218		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003125287	A1	20030703	US 2002-253132	20020924
PRAI	US 2001-324401P	P	20010924		
AB	This invention relates to the inhibition and down-regulation of survivin				

expression. The invention provides methods and antisense **oligonucleotides** for inhibiting or down-regulating survivin expression in cells and promoting apoptosis and cell necrosis.

L58 ANSWER 12 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:869055 HCAPLUS
 DN 137:379985
 TI Epidermal growth factor receptor antisense **oligonucleotides**, and use in the treatment of cancer
 IN **Agrawal, Sudhir; Kandimalla, Ekambar R.**
 PA **Hybridon, Inc., USA**
 SO PCT Int. Appl., 36 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002090514	A2	20021114	WO 2002-US14557	20020507
	WO 2002090514	C1	20040219		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2003045494	A1	20030306	US 2002-140228	20020507
	EP 1409639	A1	20040421	EP 2002-726850	20020507
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	US 2001-289055P	P	20010507		
	US 2001-289149P	P	20010507		
	WO 2002-US14557	W	20020507		
AB	Disclosed are synthetic oligonucleotides complementary to nucleic acids encoding epidermal growth factor, as are methods of their use in the treatment of cancer.				

L58 ANSWER 13 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:736889 HCAPLUS
 DN 137:273194
 TI Modulation of immunostimulatory activity of immunostimulatory **oligonucleotide** analogs by positional chemical changes
 IN **Kandimalla, Ekambar R.; Zhao, Qiuyan; Yu, Dong ; Agrawal, Sudhir**
 PA USA
 SO U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 712,898.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137714	A1	20020926	US 2001-965116	20010926 <--
PRAI	US 2000-235452P	P	20000926	<--	
	US 2000-235453P	P	20000926	<--	
	US 2000-712898	A2	20001115	<--	
OS	MARPAT 137:273194				
AB	The invention relates to the therapeutic use of oligonucleotides or oligonucleotide analogs as immunostimulatory agents in				

immunotherapy applications. The invention provides methods for enhancing the immune response caused by immunostimulatory **oligonucleotide** compds. A study of the structure-activity relationships of modified CpG **oligodeoxynucleotide phosphorothioates** was made.

L58 ANSWER 14 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:654994 HCAPLUS

DN 137:195539

TI Reversal of anti-malarial drug resistance through antisense **oligonucleotides** targeted to Plasmodium falciparum-specific pfmdr1 gene

IN Barker, Robert H., Jr.; Rapaport, Eliezer; Zamecnik, Paul C.

PA **Hybridon, Inc., USA**; Worchester Foundation for Biomedical Research

SO U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 634,588.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6440660	B1	20020827	US 1996-745485	19961112 <--
	WO 9821323	A2	19980522	WO 1997-US20590	19971112 <--
	WO 9821323	A3	19981126		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9854348	A1	19980603	AU 1998-54348	19971112 <--
PRAI	US 1995-560474	B1	19951117		<--
	US 1996-634588	A2	19960418		<--
	US 1996-745485	A	19961112		<--
	WO 1997-US20590	W	19971112		<--
AB	The present invention provides methods of resensitizing an anti-drug-resistant infectious agent to a drug. Synthetic oligonucleotides are designed having a nucleotide sequence complementary to a conserved region, an ATP-binding site, the translational start site, and a Plasmodium falciparum-specific region in the pfmdr1 gene. The oligonucleotides down-regulate the expression of pfmdr1 gene. In the presence of such oligonucleotides specific for pfmdr1, W2mef, a mefloquine-resistant strain of P. falciparum, becomes significantly more sensitive to mefloquine. This is demonstrated both by reduced total incorporation of [3H]-hypoxanthine, and in the downward shift in the threshold dose at which the parasite loses tolerance to mefloquine. These effects are specific, since mismatch control oligonucleotides do not significantly alter mefloquine sensitivity.				
RE.CNT	35	THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD			
		ALL CITATIONS AVAILABLE IN THE RE FORMAT			

L58 ANSWER 15 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:647077 HCAPLUS

DN 137:215418

TI Conjugation of Ligands at the 5'-End of CpG DNA Affects Immunostimulatory Activity

AU Kandimalla, Ekambar R.; Bhagat, Lakshmi; Yu, Dong;

Cong, Yanping; Tang, Jimmy; Agrawal, Sudhir

CS **Hybridon Inc., Cambridge, MA, 02139, USA**

SO Bioconjugate Chemistry (2002), 13(5), 966-974

CODEN: BCCHEs; ISSN: 1043-1802

PB American Chemical Society

DT Journal

LA English

AB Bacterial DNA and synthetic **oligonucleotides** containing unmethylated CpG **dinucleotides** (CpG DNA) activate the vertebrate immune system and promote Th1-like immune responses. Several CpG DNAs are currently being tested in clin. trials as either alone or in combination with vaccines, antibodies, and allergens sep. or as conjugates for a number of disease indications including cancers, allergies, and asthma. In this paper, the authors show that conjugation of an **oligonucleotide** and a CpG DNA through their 5'-ends (5'-5'-linked DNA) significantly reduces the immunostimulatory activity of the CpG DNA. In addition, the authors found that the reduction in immunostimulatory activity of 5'-5'-linked CpG DNA depends on the size of the **oligonucleotide** conjugated to CpG DNA. Conjugation of a smaller group or mol., such as a **phosphorothioate** group, at the 5'-end of CpG DNA has an insignificant effect on immunostimulatory activity. However, conjugation of a **mononucleotide**, tetra- or longer **oligonucleotide** or a fluorescein mol. to the 5'-end of a CpG DNA (5'-5'-linked DNA) significantly suppresses the immunostimulatory activity of CpG DNA. Surprisingly, conjugation of an **oligonucleotide** or a ligand through the 3'-end of CpG DNA (3'-3'-linked DNA) has an insignificant effect on immunostimulatory activity. Studies of cellular uptake and activation of transcription factor NF- κ B in J774 cells using fluorescein-conjugated CpG DNAs suggest that the differences in the immune stimulation of 5'- and 3'-end-conjugated CpG DNAs is not as a result of differences in their cellular uptake properties. These results suggest that for optimal immunostimulatory activity, ligands should not be attached at the 5'-end of the CpG DNA.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 16 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:256277 HCAPLUS

DN 136:304033

TI Modulation of immunostimulatory activity of immunostimulatory
oligonucleotide analogs by positional chemical changes

IN Kandimalla, Ekambar R.; Zhao, Quiyan; Yu, Dong; Agrawal, Sudhir

PA Hybridon, Inc., USA

SO PCT Int. Appl., 94 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002026757	A2	20020404	WO 2001-US30137	20010926 <--
	WO 2002026757	A3	20030103		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2001094750	A5	20020408	AU 2001-94750	20010926 <--
	EP 1322656	A2	20030702	EP 2001-975423	20010926 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2004509970	T2	20040402	JP 2002-531140	20010926 <--

PRAI US 2000-235452P P 20000926 <--
 US 2000-235453P P 20000926 <--
 US 2000-712898 A 20001115 <--
 WO 2001-US30137 W 20010926

OS MARPAT 136:304033

AB The invention relates to the therapeutic use of oligonucleotides or oligonucleotide analogs as immunostimulatory agents in immunotherapy applications. The invention provides methods for enhancing the immune response caused by immunostimulatory oligonucleotide compds. Examples are provided on immunostimulatory activity of oligonucleotides in mouse lymphocyte proliferation assays and in vivo on mouse spleen weight. Structure-activity relationships are discussed.

L58 ANSWER 17 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:90226 HCAPLUS

DN 136:145278

TI Use of modified **oligonucleotide** to down-regulate gene expression

IN Agrawal, Sudhir; Diasio, Robert B.; Zhang, Zhang

PA Hybridon, Inc., USA

SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002008420	A2	20020131	WO 2001-US18338	20010606 <--
	WO 2002008420	A3	20021017		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6608035	B1	20030819	US 2000-587934	20000606 <--
	US 2004033980	A1	20040219	US 2003-640898	20030814 <--
PRAI	US 2000-587934	A	20000606 <--		
	US 1994-328520	A2	19941025 <--		
	US 1996-709910	B2	19960909 <--		
	US 1996-758005	B1	19961127 <--		

AB Disclosed is a method of down-regulating the expression of a gene in an animal, wherein a pharmacol. formulation comprising a chimeric **oligonucleotide** complementary to the gene is orally administered to an animal. The **oligonucleotide** administered has at least one **phosphorothioate internucleotide** linkage and at least one **alkylphosphonate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, phosphoramidite, phosphate ester, carbamate, carbonate, phosphate triester, acetamidate, or carboxymethyl ester internucleotide** linkage.

L58 ANSWER 18 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:920765 HCAPLUS

DN 136:395476

TI The Cockayne syndrome group B DNA repair protein as an anti-cancer target

AU Lu, Yi; Mani, Sridhar; Kandimalla, Ekambar R.; Yu, Dong

; Agrawal, Sudhir; States, J. Christopher; Bregman, David B.

CS Department of Pathology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SO International Journal of Oncology (2001), 19(6), 1089-1097

CODEN: IJONES; ISSN: 1019-6439

PB International Journal of Oncology

DT Journal

LA English

AB Cells from individuals with Cockayne syndrome (CS) have a defect in transcription-coupled DNA repair (TCR), which rapidly corrects certain DNA lesions located on the transcribed strand of active genes. Despite this DNA repair defect, individuals with CS (of which there are 2 complementation groups, CSA and CSB) do not demonstrate an elevated incidence of cancer. Recently, the authors demonstrated that disruption of the CSB gene reduces the spontaneous tumor rate in cancer predisposed Ink4a/ARF-/- mice as well as causing their embryo fibroblasts to proliferate more slowly and be more sensitive to UV-induced apoptosis. In the present study the authors characterized **phosphorothioate** backbone antisense **oligodeoxynucleotides** (AOs) that reduced the levels of CSB mRNA in A2780/CP70 ovarian carcinoma cells. The AOs caused the cells to proliferate more slowly and made them more sensitive to either cisplatin or oxaliplatin. The AOs also enhanced the cytotoxicity of hydrogen peroxide and γ -radiation, both of which can induce oxidative DNA lesions, which are subject to TCR. The AOs did not potentiate the cytotoxicity of topotecan, which induces DNA strand breaks. Chemical modified ("mixed backbone") AOs (MBOs) targeting CSB were able to potentiate the anti-tumor effect of cisplatin against A2780/CP70 tumor xenografts formed in nude mice. The MBOs enabled a non-toxic (3 mg/kg) dose of cisplatin to have the same degree of anti-tumor efficacy as a more toxic (5 mg/kg) cisplatin dose. Collectively, these results suggest that the CSB gene product may be viewed as an anti-cancer target.

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 19 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:886849 HCAPLUS

DN 136:15219

TI Mixed-backbone **oligonucleotides** containing POPS blocks to obtain reduced **phosphorothioate** content

IN Zhou, Wen-Qiang; Agrawal, Sudhir

PA Can.

SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Provisional Ser. No. 80,321.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001049436	A1	20011206	US 1999-283431	19990401 <--
	US 2003220486	A1	20031127	US 2002-291058	20021108 <--
PRAI	US 1998-80321P	P	19980401 <--		
	US 1999-283431	A1	19990401 <--		

AB Mixed-backbone **oligonucleotides** POPS blocks have been designed and studied for their target affinity, nuclease stability in vitro and in vivo, RNase H-activation properties, and their effect on **phosphorothioate**-related prolongation of partial thromboplastin time, in an effort to have agents with improved antisense activity with reduced **phosphorothioate** content. POPS blocks are **oligonucleotide** regions containing alternating **nucleoside phosphodiester**s (PO) and **nucleoside phosphorothioates** (PS).

L58 ANSWER 20 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:816684 HCAPLUS

DN 135:352788

TI Modulation of oligonucleotide CpG-mediated immune stimulation by

positional modification of nucleosides

IN Agrawal, Sudhir
 PA Hybridon, Inc., USA
 SO PCT Int. Appl., 27 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001083503	A2	20011108	WO 2001-US13682	20010430 <--
	WO 2001083503	A3	20020718		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1278761	A2	20030129	EP 2001-930870	20010430 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2003531915	T2	20031028	JP 2001-580927	20010430 <--
PRAI	US 2000-201578P	P	20000501 <--		
	WO 2001-US13682	W	20010430		

OS MARPAT 135:352788

AB The invention provides methods for modulating the immune response caused by CpG dinucleotide-containing compds. The methods according to the invention enable both decreasing the immunostimulatory effect for antisense applications, as well as increasing the immunostimulatory effect for immunotherapy applications.

L58 ANSWER 21 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:815865 HCAPLUS

DN 136:128431

TI Antisense and/or immunostimulatory oligonucleotide therapeutics

AU Agrawal, Sudhir; Kandimalla, Ekambar R.

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Current Cancer Drug Targets (2001), 1(3), 197-209

CODEN: CCDTB9; ISSN: 1568-0096

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. Antisense technol., which is based on a simple and rational principle of Watson-Crick complementary base pairing of a short **oligonucleotide** with the targeted mRNA to downregulate the disease-causing gene product, has progressed tremendously in the last two decades. Antisense **oligonucleotides** targeted to a number of cancer-causing genes are being evaluated in human clin. trials. While the first-generation **phosphorothioate** antisense **oligonucleotides** are in clin. trials, a number of factors, including sequence motifs that could lead to unwanted mechanisms of action and side effects, have been identified. The severity of the side effects of first-generation antisense **oligonucleotides** is mostly dependent on the presence of certain sequence motifs, such as CpG **dinucleotides**. A number of second-generation chemical modifications have been proposed to overcome the limitations of the first-generation antisense **oligonucleotides**. The safety and efficacy of several second-generation mixed-backbone antisense **oligonucleotides** are being evaluated in clin. trials. The immune stimulation effects observed with CpG-containing antisense **oligonucleotides** are being exploited

as a novel therapeutic modality, with several CpG **oligonucleotides** being evaluated in clin. trials. A number of medicinal chemical studies performed to date suggest that the immunomodulatory activity of CpG **oligonucleotides** can be fine-tuned by site-specific incorporation of chemical modifications in order to design disease-specific **oligonucleotide** therapeutics.

RE.CNT 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 22 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:747595 HCAPLUS

DN 135:322693

TI Sensitization of cells to cytotoxic agents using **oligonucleotides** directed to **nucleotide** excision repair or transcription-coupled repair genes

IN Agrawal, Sudhir; Kandimalla, Ekambar R.; Bregman, David B.; Mani, Sridhar; Lu, Yi

PA Hybridon, Inc., USA

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074346	A2	20011011	WO 2001-US10800	20010403 <--
	WO 2001074346	A3	20020725		
	W:		AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
EP	1267933	A2	20030102	EP 2001-923091	20010403 <--
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
PRAI	US 2000-194343P	P	20000403 <--		
	WO 2001-US10800	W	20010403		
AB	This invention relates to the fields of mol. biol. and oncol. More particularly, this invention relates to the sensitization of cancerous cells to therapeutic agents. The invention provides methods, compns., and formulations for potentiating or enhancing the toxicity of various cytotoxins and oxidizing agents, and of reducing the resistance and proliferation rate of cancer cells. It also provides various compns. and therapeutic formulations useful as anticancer agents in targeting xeroderma pigmentosum and Cockayne's syndrome genes.				

L58 ANSWER 23 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:565246 HCAPLUS

DN 135:148194

TI Modulation of CpG-**oligonucleotide** mediated immune stimulation and mammalian gene expression by positional modification of **nucleosides**

IN Agrawal, Sudhir

PA Hybridon, Inc., USA

SO PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001055370	A2	20010802	WO 2001-US2681	20010126 <--
	WO 2001055370	A3	20020117		
	WO 2001055370	C2	20021017		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2002055475	A1	20020509	US 2001-770602	20010126 <--
	EP 1252307	A2	20021030	EP 2001-903365	20010126 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2003520811	T2	20030708	JP 2001-554399	20010126 <--
	US 2003186912	A1	20031002	US 2002-314647	20021209 <--
PRAI	US 2000-178562P	P	20000126 <--		
	US 2001-770602	A3	20010126		
	WO 2001-US2681	W	20010126		

AB The invention provides methods for modulating the immune response caused by CpG-containing **oligonucleotides**. The methods according to the invention enable both decreasing the immunostimulatory effect for antisense applications, as well as increasing the immunostimulatory effect for immunotherapy applications. The present inventor has surprisingly discovered that positional modification of CpG-containing **oligonucleotides** dramatically affects their immunostimulatory capabilities. In particular, 3' alkylation or alkoxylation of **oligonucleotides**, or introduction of an uncharged **internucleoside** linkage, at particular positions 5' or 3' to the CpG **dinucleotide** either enhances or reduces their immunostimulatory effect in a reproducible and predictable manner. Substitution with 3'-O-Me **ribonucleosides** in Oligos 2-5 simultaneously led to incorporation of 2'-5' **internucleoside** linkages. Substitution 5' of the CpG with no intervening **nucleosides** (Oligo 2) diminished immunostimulatory activity. Surprisingly, substitution 3' of the CpG with no intervening **nucleosides** (Oligo 5) also diminished immunostimulatory activity. In addition, Oligos 3 and 4, with 3'-O-**methylribonucleoside** substitution 3' to the CpG increase immunostimulatory activity. **Oligonucleotides** were prepared having methylphosphonate linkages 3 or 4 **nucleotides** 5' to the CpG **dinucleotide**, or 2 or 3 **nucleotides** 3' to the CpG **dinucleotide**. As shown in Figure 3, all of these **oligonucleotides** were more immunostimulatory in both the mouse spleen cell proliferation assay and the spleen enlargement assay.

L58 ANSWER 24 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:359749 HCAPLUS
 DN 134:361390
 TI Polyanion co-administration for potentiation of prodrug efficacy
 IN Agrawal, Sudhir
 PA Hybridon, Inc., USA
 SO PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2001034093 A2 20010517 WO 2000-US30687 20001108 <--
 WO 2001034093 A3 20011122
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 2001014749 A5 20010606 AU 2001-14749 20001108 <--
 EP 1229938 A2 20020814 EP 2000-977058 20001108 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2003513894 T2 20030415 JP 2001-536098 20001108 <--
 PRAI US 1999-164182P P 19991109 <--
 WO 2000-US30687 W 20001108 <--
 AB The invention provides methods for statistically significantly
 potentiating the activity of a prodrug, e.g. an anticancer prodrug,
 without producing significant side effects, the method comprising
 co-administering a polyanion, e.g. a polysulfate or
oligonucleotide, with the prodrug.
 L58 ANSWER 25 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:340137 HCAPLUS
 DN 135:313249
 TI Potentiation of antitumor activity of irinotecan by chemically modified
oligonucleotides
 AU Agrawal, Sudhir; Kandimalla, Ekambar R.; Yu,
 Dong; Hollister, Beth A.; Chen, Shih-Fong; Dexter, Daniel L.; Alford,
 Terri L.; Hill, Brenda; Bailey, Karen S.; Bono, Christine P.; Knoerzer,
 Deborah L.; Morton, Phillip A.
 CS Hybridon, Inc., Cambridge, MA, 02139, USA
 SO International Journal of Oncology (2001), 18(5), 1061-1069
 CODEN: IJONES; ISSN: 1019-6439
 PB International Journal of Oncology
 DT Journal
 LA English
 AB Co-administration of synthetic chemical modified **oligonucleotides**
 with irinotecan, a selective topoisomerase I inhibitor, provided an
 enhancement in the antitumor activity of irinotecan. The enhancement of
 antitumor activity of irinotecan with co-administration of chemical modified
oligonucleotides was observed in several tumor models - pancreatic
 cancer (Panc-1), colon cancer (HCT-116), and melanoma (A375). Inhibition
 of tumor growth in all 3 models required the co-administration of
 irinotecan and chemical modified **oligonucleotides**, but was
 independent of the **nucleotide** sequence of the
oligonucleotides. The potentiation of antitumor activity was
 dependent on the dose of irinotecan and chemical modified
oligonucleotides administered. The enhancement of antitumor
 activity of irinotecan was also observed by co-administration of a
phosphorothioate oligonucleotide, however, to a lesser
 extent than did chemical modified **oligonucleotides**, suggesting that
 metabolic stability of the **oligonucleotide** contributes to the
 enhancement of antitumor activity seen with irinotecan. The
 co-administration of dextran sulfate sodium with irinotecan showed
 insignificant potentiation of antitumor activity of irinotecan, suggesting
 that the enhancement of antitumor activity of irinotecan observed was not a
 result of polyanionic characteristic of **oligonucleotides**.
 Co-administration of irinotecan and chemical modified
oligonucleotides did not result in increased toxicity in the tumor
 models studied. Potentiation of antitumor activity of irinotecan observed

with co-administration of **oligonucleotides** suggests that the **oligonucleotides** affect the pharmacokinetics and/or metabolism of irinotecan. The use of chemical modified **oligonucleotides** together with irinotecan may increase the therapeutic index of irinotecan in cancer patients and continued development of such agents should be considered.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 26 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:322284 HCAPLUS

DN 135:174657

TI Effect of chemical modifications of cytosine and guanine in a CpG-motif of **oligonucleotides**: structure-immunostimulatory activity relationships

AU Kandimalla, Ekambar R.; Yu, Dong; Zhao, Qiuyan
; Agrawal, Sudhir

CS Hybridon Inc., Cambridge, MA, 02139, USA

SO Bioorganic & Medicinal Chemistry (2001), 9(3), 807-813

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

AB **Oligodeoxynucleotides** containing unmethylated CpG-motifs stimulate the innate immune system, including inducing B-cell proliferation and cytokine production. However, the mechanism of immunostimulation by CpG-**oligonucleotides** and the precise structural requirements and specific functional groups of cytosine and guanine necessary for recognition of and interaction with protein/receptor factors that are responsible for immune stimulation have not been elucidated. We sought to understand the critical role of each functional group of the cytosine and guanine moieties in a CpG-motif in inducing immunostimulatory activity. To this end, we examined structure-immunostimulatory activity relationships of **phosphorothioate oligodeoxynucleotides** (PS-oligos) containing YpG- and CpR-motifs (Y and R stand for pyrimidine and purine analogs, resp.). The PS-oligos containing a YpG-motif in which the natural deoxycytidine was replaced with deoxy-5-hydroxycytidine or deoxy-N4-ethylcytidine showed immunostimulatory activity. Substitution of deoxycytidine with a deoxy-5-methylisocytidine, deoxyuridine, or deoxy-P-base-**nucleoside** in the YpG-motif completely abolished the immunostimulatory activity, similar to the results observed with deoxy-5-methylcytidine. In the case of PS-oligos containing a CpR-motif, 7-deazaguanine substitution for natural guanine showed immunostimulatory activity similar to that of a parent PS-oligo. These studies suggest that the 2-keto, 3-imino and 4-amino groups of cytosine, and the 1-imino, 2-amino and 6-keto groups of guanine in a CpG-motif are important for the immunostimulatory activity of CpG-PS-oligos. The absence of N7 on guanine of the CpG-motif does not affect immunostimulatory activity significantly. These studies suggest that it is possible to develop YpG- and CpR-motifs as an alternative to CpG-motifs in PS-oligos for immunostimulatory studies.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 27 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:77057 HCAPLUS

DN 134:260930

TI Non-specific antiviral activity of antisense molecules targeted to the E1 region of human papillomavirus

AU Lewis, E. Jonathan; Agrawal, Sudhir; Bishop, Jill; Chadwick, Jenny; Cristensen, Neil D.; Cuthill, Scott; Dunford, Paul; Field, A. Kirk; Francis, John; Gibson, Vivien; Greenham, Anna K.; Kelly, Fiona; Kilkushie, Robert; Kreider, John W.; Mills, John S.; Mulqueen, Michael; Roberts, Noel A.; Roberts, Peter; Szymkowski, David E.

CS Roche Discovery Welwyn, Welwyn Garden City, AL7 3AY, UK
SO Antiviral Research (2000), 48(3), 187-196
CODEN: ARSRDR; ISSN: 0166-3542
PB Elsevier Science B.V.
DT Journal
LA English
AB Antisense **phosphorothioate oligonucleotides** (ODN1 0+5 OMe) directed against the E1 start region of human papillomavirus 11 (HPV11) can inhibit papillomavirus induced growth of implanted human foreskin in a mouse xenograft model. Administration of a mismatch control **oligonucleotide** (ODN9 0+5 OMe), in which guanine was replaced with adenine in the same model, had no effect on papilloma induced growth. However, the apparent antiviral activity of ODN1 0+5 OMe was also shown in a lethal mouse cytomegalovirus (CMV) model, in which the **oligonucleotides** are not expected to have antisense activity. To understand the mechanisms of action of these **oligonucleotides**, a mismatch **oligonucleotide** (ODN61 0+5 OMe) was prepared which retained the CpG motifs of ODN1 0+5 OMe. This was tested in the mouse xenograft model and shown to have moderate inhibitory activity. As a definitive experiment, a comparison was made between the efficacy of the active **oligonucleotide** ODN1 0+5 OMe against two papilloma viruses HPV11 and HPV40. Both these viruses cause benign genital warts, but differ by four bases in their E1 sequence that was the target for ODN1 0+5 OMe. Papillomavirus induced growth in the mouse xenograft model was inhibited by ODN1 0+5 OMe in both cases, suggesting that **oligonucleotide** mols. have a non-specific antiviral activity that is not directly related to their antisense sequence.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 28 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:832449 HCAPLUS
DN 134:231490
TI Accessible 5'-end of CpG-containing **Phosphorothioate Oligodeoxynucleotides** is essential for immunostimulatory activity
AU Yu, D.; Zhao, Q.; Kandimalla, E. R.; Agrawal, S.
CS Hybridon, Inc., Cambridge, MA, 02139, USA
SO Bioorganic & Medicinal Chemistry Letters (2000), 10(23), 2585-2588
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB In the authors ongoing efforts to decipher the sequence and structural requirements in the flanking region of the CpG motif in **phosphorothioate oligodeoxynucleotides** (PS-oligos), the authors have examined the requirement of free 5'- and 3'-ends of PS-oligos on immune stimulation. Our model studies using 3'-3'-linked (containing two free 5'-ends) and 5'-5'-linked (containing two free 3'-ends) CpG-containing PS-oligos demonstrate that immunostimulatory activity is significantly reduced when the 5'-end of the PS-oligo is not accessible, rather than the 3'-end, suggesting that the 5'-end plays a critical role in immunostimulatory activity.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 29 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:659279 HCAPLUS
DN 134:27148
TI Polymer solutions as a pseudostationary phase for capillary electrochromatographic separation of DNA diastereomers

AU Gilar, Martin; Belenky, Alexei; Cohen, Aharon S.

CS Hybridon, Milford, MA, USA

SO Electrophoresis (2000), 21(14), 2999-3009

CODEN: ELCTDN; ISSN: 0173-0835

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

AB The solns. of linear polymers traditionally used for DNA separation have been employed for the capillary electrophoresis (CE) of diastereomers of chemical modified DNA. The selectivity of diastereomeric separation of the phosphorothioate (PS) and 2'-O-methylated (2-OMe) PS oligonucleotides depends on the nature of the polymer additive in the CE background electrolyte. The selectivity of separation for different polymers increases in the line: linear polyacrylamide < polyethylene glycol < polyvinyl pyrrolidone. The separation of oligomer diastereomers was shown to be primarily based on the hydrophobic interaction with the polymer network that acts as a pseudostationary phase. While lowering the temperature resulted in improved separation, the addition of organic modifiers such as formamide, methanol

or acetonitrile counteracts the solute adsorption on the polymer network, and decreases the selectivity of DNA diastereo-separation. The effect of mol. mass and concentration of the polymer on the separation selectivity was

investigated.

IT 155487-47-1 183506-04-9 311310-93-7

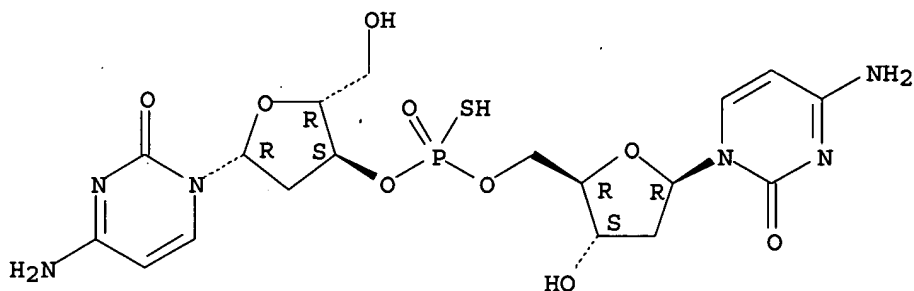
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)

(polymer solns. as a pseudostationary phase for capillary electrochromatog. separation of DNA diastereomers)

RN 155487-47-1 HCAPLUS

CN Cytidine, 2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy- (9CI) (CA INDEX NAME)

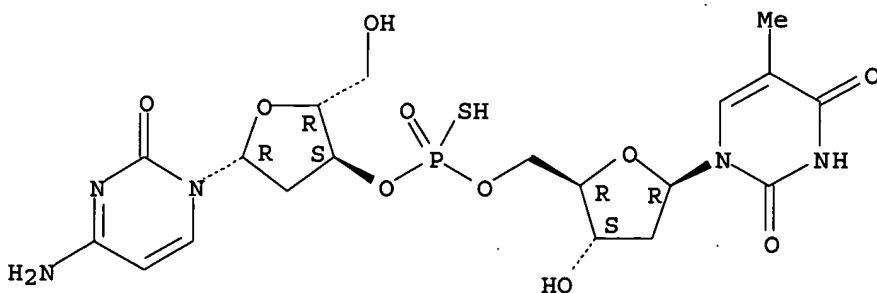
Absolute stereochemistry.



RN 183506-04-9 HCAPLUS

CN Thymidine, 2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

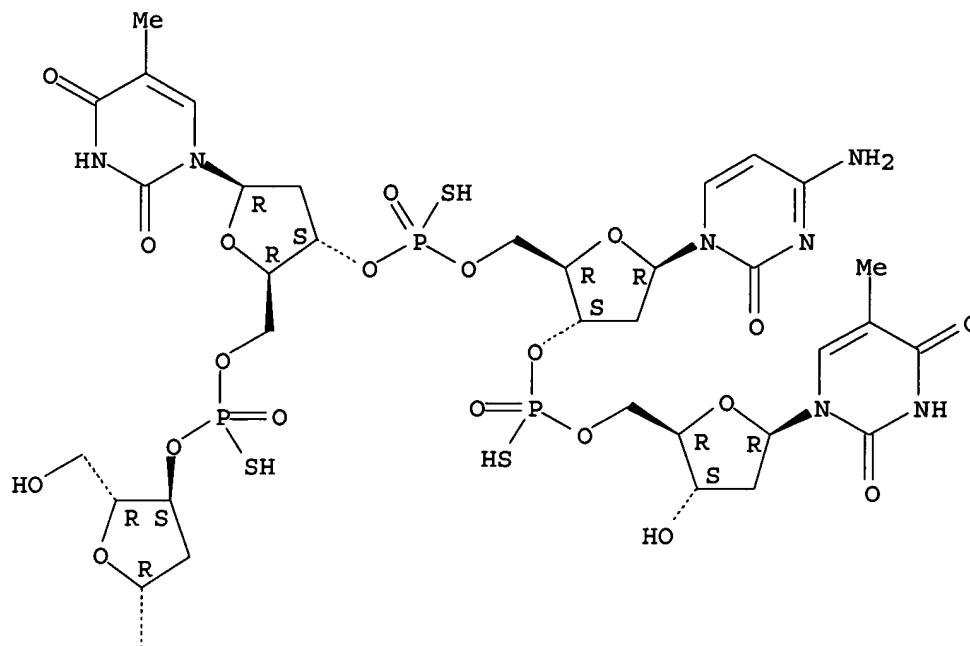
Absolute stereochemistry.



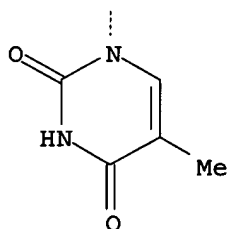
RN 311310-93-7 HCAPLUS
 CN Thymidine, P-thiothymidylyl-(3'→5')-P-thiothymidylyl-(3'→5')-
 2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

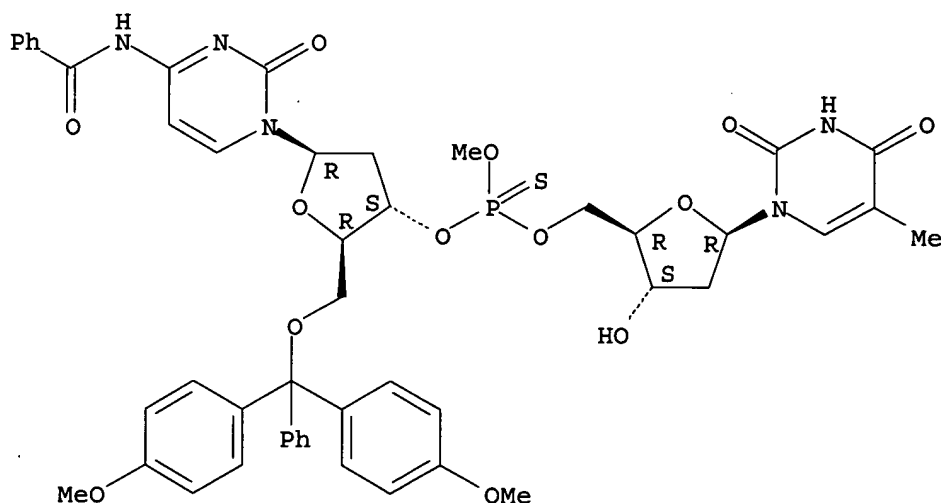


RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 30 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:470321 HCAPLUS
 DN 133:89748
 TI Extremely high purity oligonucleotides and methods of synthesizing them
 using dimer blocks
 IN Tang, Jin-yan; Bongle, Nandkumar; Gonzalez, Jose; Schwartz, Warren E.
 PA Hybridon, Inc., USA
 SO U.S., 18 pp., Cont.-in-part of U.S. Ser. No. 339,918, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 2

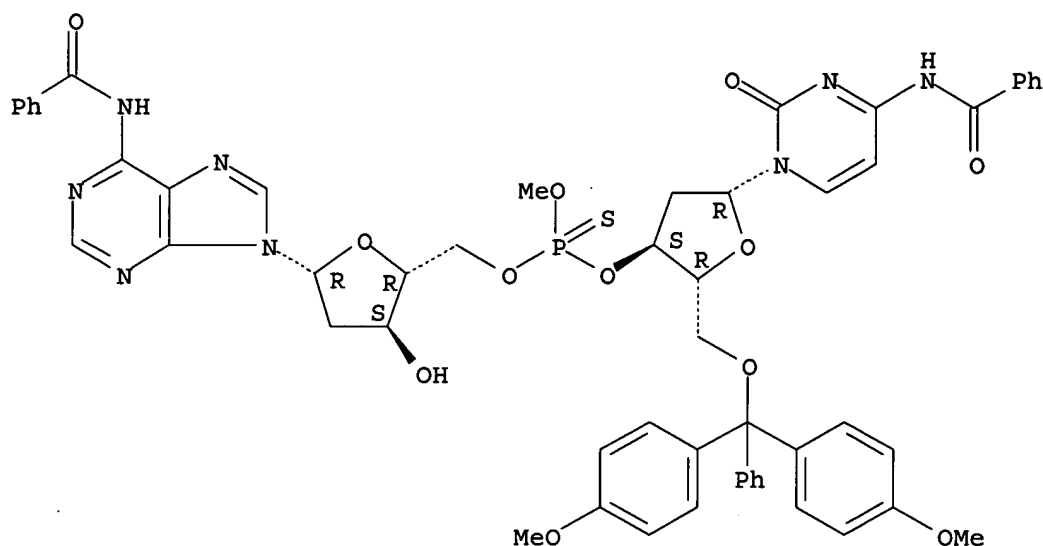
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6087491	A	20000711	US 1997-827561	19970502
	US 6310198	B1	20011030	US 2000-545273	20000407
PRAI	US 1993-2823	B1	19930108		
	US 1994-339918	B2	19941115		
	US 1997-827561	A1	19970502		
OS	MARPAT 133:89748				
AB	The present invention comprises an improved method of synthesizing oligonucleotides employing dinucleotides (or "dimer blocks") as the basic synthetic unit building block. The method results in extremely high purity oligonucleotides in which the N-1 content is very low, generally less than 1-2% of the full length, N, oligonucleotide. Use of dinucleotide phosphorothioates results in oligonucleotides having very little phosphodiester content. Furthermore, the amount of dimer required in each coupling step can be less than about 6 and is preferably about 2 equivalent. Synthesis of oligonucleotides according to the dimer block approach described herein can also be conducted without the capping step that has heretofore been deemed necessary after each coupling. Thus, 5'-O-dimethoxytritylthymidine-3'-O-Me N,N-diisopropylphosphoramidite and N4-benzoyl-3'-O-(tert-butyldimethylsilyl)-2'-deoxycytidine were combined with MeCN, tetrazole, and Beaucage reagent to give in 2 steps the title dimer 5'-O-(dimethoxytrityl)thymidine-3'-O-Me phosphorothioate-5'-O-N4-benzoyl-2'-deoxycytidine in 70% yield.				
IT	162431-92-7P 162431-93-8P 280113-37-3P				
	RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)				
	(extremely high purity oligonucleotides and methods of synthesizing them using dimer blocks)				
RN	162431-92-7 HCAPLUS				
CN	Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



RN 162431-93-8 HCAPLUS
 CN Adenosine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')-N-benzoyl-2'-deoxy- (9CI) (CA INDEX NAME)

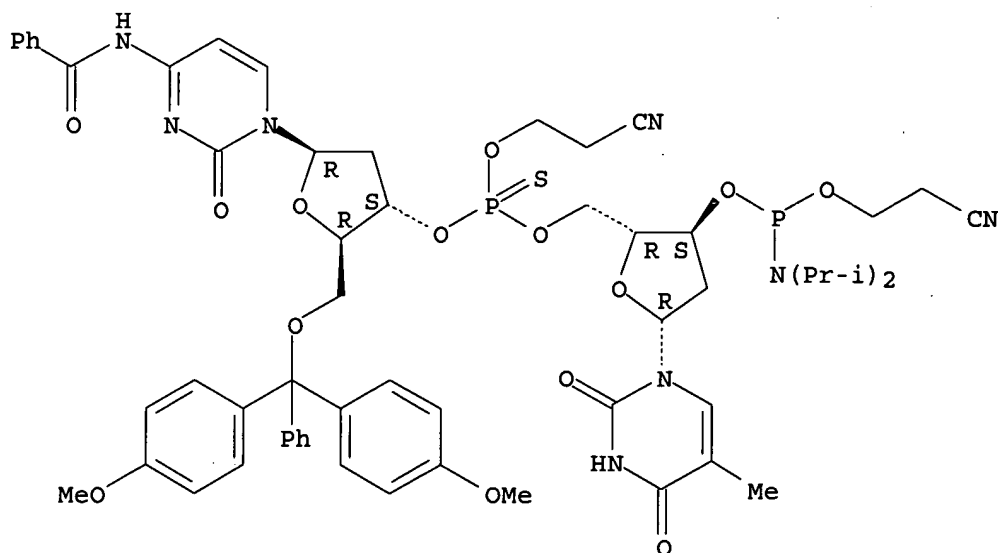
Absolute stereochemistry.



RN 280113-37-3 HCAPLUS

CN Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P(O)-(2-cyanoethyl)-2'-deoxy-P-thiocytidylyl-(3'→5')-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



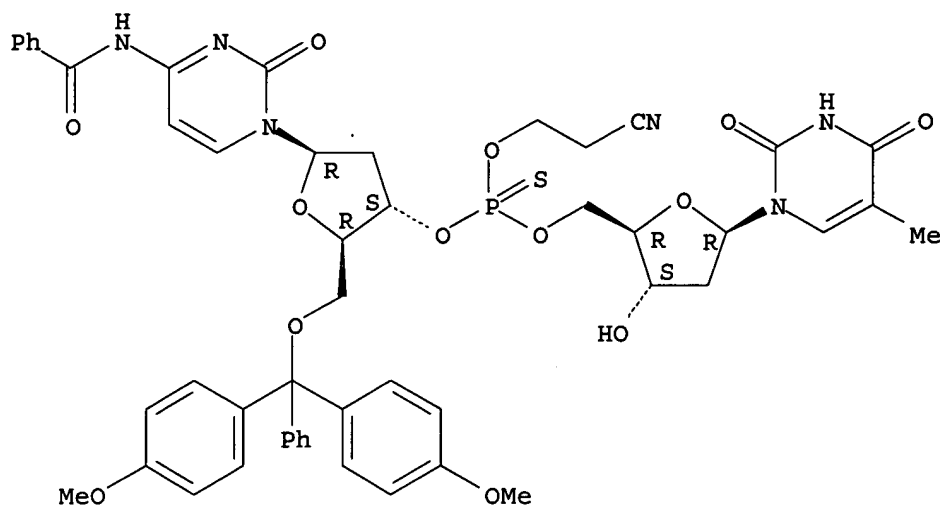
IT 162491-21-6P 191171-96-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(extremely high purity oligonucleotides and methods of synthesizing them using dimer blocks)

RN 162491-21-6 HCAPLUS

CN Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P(O)-(2-cyanoethyl)-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

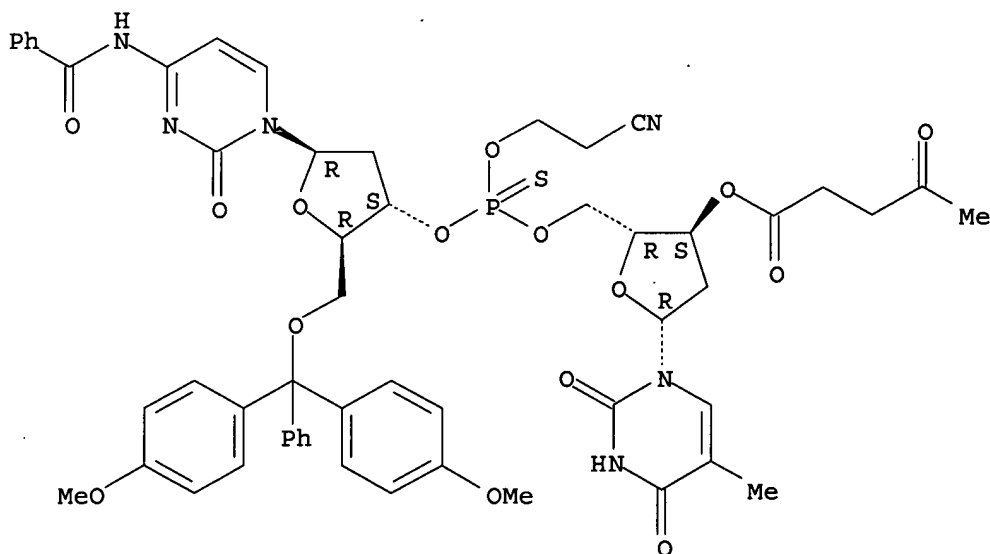
Absolute stereochemistry.



RN 191171-96-7 HCAPLUS

CN Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P(O)-(2-cyanoethyl)-2'-deoxy-P-thiocytidyl-(3'→5')-, 3'-(4-oxopentanoate)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 31 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:286659 HCAPLUS

DN 133:99027

TI Intratumoral pharmacokinetics of **oligonucleotides** in a tissue-isolated tumor perfusion system

AU Nakajima, Shin; Koshino, Yasuaki; Nomura, Takehiko; Yamashita, Fumiyoshi; **Agrawal, Sudhir**; Takakura, Yoshinobu; Hashida, Mitsuru

CS Department of Drug Delivery Research, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan

SO Antisense & Nucleic Acid Drug Development (2000), 10(2), 105-110
CODEN: ANADF5; ISSN: 1087-2906

PB Mary Ann Liebert, Inc.

DT Journal

LA English

AB The intratumoral pharmacokinetics of model **oligonucleotides** were studied in Walker 256 tissue-isolated tumor prepns. using an in situ single-pass vascular perfusion technique. A 20-mer **phosphodiester (PO) oligonucleotide**, its fully **phosphorothioated (PS) oligonucleotide** counterpart, and an 18-mer **phosphorothioated oligonucleotide** containing four 2'-O-methylribonucleosides at both the 3'-end and 5'-end (PS-OMe) were used. These **oligonucleotides** were administered to the tumor in two ways, by constant arterial infusion and by direct intratumoral injection. In the case of constant arterial infusion, the expts. were carried out using perfusate with or without 4.7% bovine serum albumin (BSA). The protein binding of PO, PS, and PS-OMe to BSA was 46%, 87%, and 94%, resp. No marked difference was observed between the degree of accumulation of the three types of **oligonucleotides** in the tumor when BSA was present in the perfusate. PS and PS-OMe showed higher degrees of accumulation in tumors compared with PO when no BSA was present. These results indicate that free (i.e., protein unbound) PS-OMe and PS have superior tumor accumulation characteristics. In the intratumoral injection expts., PS-OMe was retained longer in tumor tissue compared with PS, suggesting that it might be useful for direct local injection into solid tumors. Thus, the present study provides useful information about the basic disposition characteristics of **oligonucleotides** in solid tumors.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 32 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:125876 HCAPLUS

DN 132:308589

TI Stereo-enriched phosphorothioate oligodeoxynucleotides: synthesis, biophysical and biological properties

AU Yu, Dong; Kandimalla, Ekambar R.; Roskey, Allysen; Zhao, Qiuyan; Chen, Lihong; Chen, Jiangdong; Agrawal, Sudhir

CS Hybridon, Inc., Milford, MA, 01757, USA

SO Bioorganic & Medicinal Chemistry (2000), 8(1), 275-284
CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

AB Stereo-enriched [Rp] and [Sp]-phosphorothioate oligodeoxynucleotides are synthesized using oxazaphospholidine derivatized monomers. Three different designs of phosphorothioate oligodeoxynucleotides (PS-oligos), (i) stereo-enriched all-[Rp] or all-[Sp] PS-linkages, (ii) stereo-random mixture of PS-linkages, and (iii) segments containing certain number of stereo-enriched [Rp] and [Sp] PS-linkages ([Sp-Rp-Sp] or [Rp-Sp-Rp]), have been studied. Thermal melting studies of these PS-oligos with RNA complementary strands showed that the binding affinities are in the order [Rp] > [Sp-Rp-Sp] = [Rp-Sp-Rp] > stereo-random > [Sp]. CD (CD) studies suggest that the stereochem. of the PS-oligo does not affect the global conformation of the duplex. The in vitro nuclease stability of these PS-oligos is in the order [Sp] > [Sp-Rp-Sp] > stereo-random > [Rp]. The RNase H activation is in the order [Rp] > stereo-random > [Rp-Sp-Rp] > [Sp] > [Sp-Rp-Sp]. Studies in a cancer cell line of PS-oligos targeted to MDM2 mRNA showed that all oligos had similar biol. activity under the exptl. conditions employed. Protein- and enzyme-binding studies showed insignificant stereo-dependent binding to proteins. The [Sp] and [Sp-Rp-Sp] chimeric and stereo-random PS-oligos that contained a CpG motif showed higher cell proliferation than [Rp] PS-oligo of the same sequence.

IT 116113-27-0P 116182-01-5P

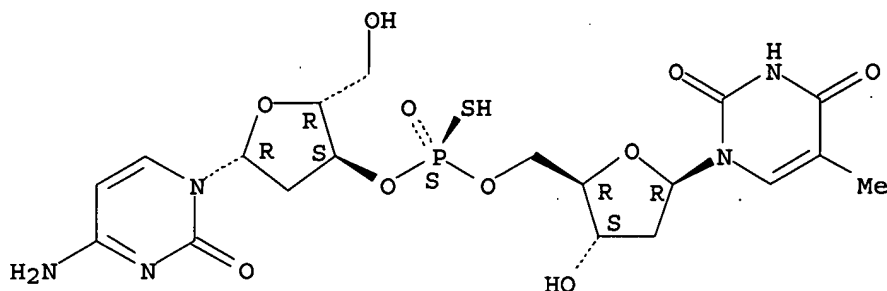
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis biophys. and biol. properties of stereo-enriched phosphorothioate oligodeoxyribonucleotides)

RN 116113-27-0 HCAPLUS

CN Thymidine, [P(S)]-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

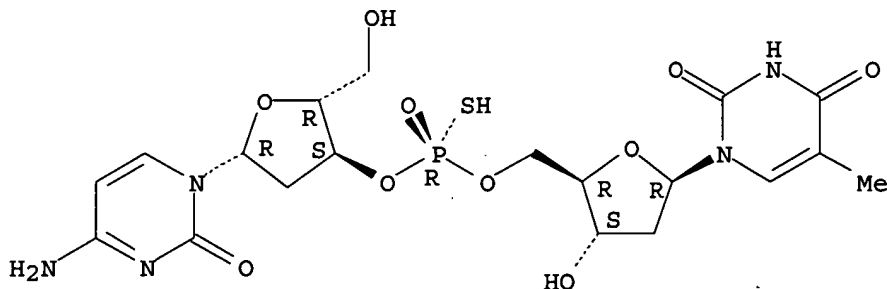
Absolute stereochemistry.



RN 116182-01-5 HCAPLUS

CN Thymidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 33 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:94981 HCAPLUS

DN 132:279454

TI Large-Scale Synthesis of Oligonucleotide Phosphorothioates Using 3-Amino-1,2,4-dithiazole-5-thione as an Efficient Sulfur-Transfer Reagent

AU Tang, Jin-Yan; Han, Yongxin; Tang, Jimmy X.; Zhang, Zhaoda

CS Hybridon Inc., Milford, MA, 01757, USA

SO Organic Process Research & Development (2000), 4(3), 194-198

CODEN: OPRDFK; ISSN: 1083-6160

PB American Chemical Society

DT Journal

LA English

AB A com. available and inexpensive compound, 3-amino-1,2,4-dithiazole-5-thione (ADTT), is discovered to be a new sulfur-transfer reagent for solid-phase synthesis of oligonucleotide phosphorothioates via the phosphoramidite method. The efficiency of ADTT was investigated by solid-phase syntheses of dinucleotide and oligonucleotide phosphorothioates. The results show that ADTT is a highly efficient sulfur-transfer reagent and fully compatible with automated solid-phase synthesis. ADTT has been applied in manufacture of oligonucleotide phosphorothioates to reduce the cost

significantly.

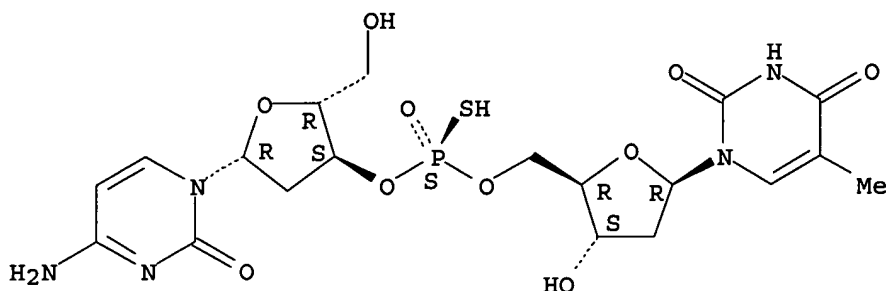
IT 116113-27-0P 116182-01-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(large-scale synthesis of oligonucleotide phosphorothioates using
aminodithiazolethione as an efficient sulfur-transfer reagent)

RN 116113-27-0 HCAPLUS

CN Thymidine, [P(S)]-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA
INDEX NAME)

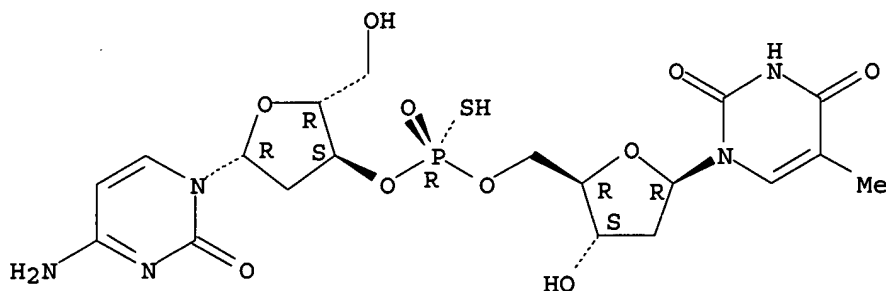
Absolute stereochemistry.



RN 116182-01-5 HCAPLUS

CN Thymidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 34 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:31378 HCAPLUS

DN 132:88168

TI Tumor suppressor-activating MDM2-specific antisense
oligonucleotides

IN Chen, Jiandong; Agrawal, Sudhir; Zhang, Ruiwen

PA Hybridon, Inc., USA

SO U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 916,384.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6013786	A	20000111	US 1998-73567	19980506 <--
	CA 2301816	AA	19990304	CA 1998-2301816	19980818 <--
	AU 9890237	A1	19990316	AU 1998-90237	19980818 <--
	EP 1007658	A2	20000614	EP 1998-942115	19980818 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

JP 2001513996 T2 20010911 JP 2000-507794 19980818 <--
 US 2003119765 A1 20030626 US 2000-541848 20000403 <--
 PRAI US 1997-916384 A2 19970822 <--
 US 1998-73567 A 19980506 <--
 WO 1998-US17147 W 19980818 <--
 US 1999-383507 A2 19990826 <--
 AB The invention provides methods to activate tumor suppressors. The invention further provides antisense **oligonucleotides** complementary to a portion of the MDM2-encoding RNA and methods for using such antisense **oligonucleotides** as anal. and diagnostic tools, as potentiators of transgenic animal studies and for gene therapy approaches, and as potential therapeutic agents. The invention also provides methods to augment and synergistically activate a tumor suppressor in conjunction with the use of a DNA-damage inducing agent.
 RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 35 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:9750 HCAPLUS
 DN 132:246043
 TI Site of chemical modifications in CpG containing **phosphorothioate oligodeoxynucleotide** modulates its immunostimulatory activity
 AU Zhao, Qiuyan; Yu, Dong; Agrawal, Sudhir
 CS Hybridon, Inc., Milford, MA, 01757, USA
 SO Bioorganic & Medicinal Chemistry Letters (1999), 9(24), 3453-3458
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 AB **Phosphorothioate oligodeoxynucleotides** containing CpG motifs have immunostimulatory activity. Appropriate substitution of **deoxynucleosides** in the flanking region of CpG-containing **phosphorothioate oligodeoxynucleotides** with 2'-O-methylribonucleosides results in significant decreases or increases in their immunostimulatory activities. The results provide insights in how to chemical modify **phosphorothioate oligodeoxynucleotides** containing CpG motifs to suppress or enhance their immunostimulatory activity for different therapeutic uses.
 RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 36 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:760673 HCAPLUS
 DN 132:160699
 TI Importance of **nucleotide** sequence and chemical modifications of antisense **oligonucleotides**
 AU Agrawal, S.
 CS Hybridon, Inc., Milford, MA, USA
 SO Biochimica et Biophysica Acta (1999), 1489(1), 53-67
 CODEN: BBACAQ; ISSN: 0006-3002
 PB Elsevier Science B.V.
 DT Journal; General Review
 LA English
 AB A review with 104 refs. The antisense approach is conceptually simple and elegant; to design an inhibitor of a specific mRNA, one needs only to know the sequence of the targeted mRNA and an appropriately modified complementary **oligonucleotide**. Of the many analogs of **oligodeoxynucleotides** explored as antisense agents, **phosphorothioate** analogs have been studied the most extensively. The use of **phosphorothioate oligodeoxynucleotides** as antisense agents in various studies have shown promising results.

However, they have also indicated that quite often, biol. effects observed could be solely or partly non-specific in nature. It is becoming clear that not all **phosphorothioate oligodeoxynucleotides** of varying length and base composition are the same, and important consideration should be given to maintain antisense mechanisms while identifying effective antisense **oligonucleotides**. In this review, I have summarized the progress made in my laboratory in understanding the specificity and mechanism of actions of **phosphorothioate oligonucleotides** and the rationale for designing second-generation mixed-backbone **oligonucleotides**.

RE.CNT 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 37 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:670137 HCAPLUS

DN 131:295574

TI Modified protein kinase A-specific **oligonucleotides**, and uses thereof in cancer therapy

IN Agrawal, Sudhir

PA Hybridon, Inc., USA

SO U.S., 13 pp., Cont.-in-part of U.S. 5,652,356.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5969117	A	19991019	US 1995-532979	19950922 <--
	US 5652356	A	19970729	US 1995-516454	19950817 <--
	CA 2229811	AA	19970227	CA 1996-2229811	19960816 <--
	EP 1340765	A2	20030903	EP 2003-10207	19960816 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	PT 1019428	T	20031031	PT 1996-930536	19960816 <--
	ES 2201198	T3	20040316	ES 1996-930536	19960816 <--
	CA 2232724	AA	19970327	CA 1996-2232724	19960919 <--
	WO 9711171	A1	19970327	WO 1996-US15084	19960919 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
	AU 9672412	A1	19970409	AU 1996-72412	19960919 <--
	EP 846170	A1	19980610	EP 1996-933833	19960919 <--
	EP 846170	B1	20010718		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11512601	T2	19991102	JP 1996-512911	19960919 <--
	AT 203271	E	20010815	AT 1996-933833	19960919 <--
	US 5773601	A	19980630	US 1997-886860	19970701 <--
	US 5973136	A	19991026	US 1997-886670	19970701 <--
	US 6624293	B1	20030923	US 1998-22965	19980212 <--
	US 2004106570	A1	20040603	US 2003-641521	20030815 <--
PRAI	US 1995-516454	A2	19950817	<--	
	US 1995-532979	A	19950922	<--	
	EP 1996-930536	A3	19960816	<--	
	WO 1996-US15084	W	19960919	<--	
	US 1997-40740P	P	19970312	<--	
	US 1998-22965	A3	19980212	<--	
AB	The invention relates to the inhibition of the proliferation of cancer cells using modified antisense oligonucleotides . Disclosed are				

synthetic, modified **oligonucleotides** complementary to, and capable of down-regulating the expression of, the gene encoding protein kinase A subunit RI60. Said **oligonucleotides** demonstrate reduced mitogenicity, reduced activation of complement, and reduced antithrombotic properties, relative to conventional **oligonucleotides**. The modified **oligonucleotides** have from about 15 to about 30 **nucleotides** and are hybrid, inverted hybrid, or inverted chimeric **oligonucleotides**. In some embodiments, the 3' and 5' flanking **ribonucleotide** regions of an **oligonucleotide** of the invention comprise 2'-O-substituted **ribonucleotides**. Also disclosed are therapeutic compns. containing such **oligonucleotides** and methods of using the same.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 38 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:548316 HCAPLUS

DN 131:282762

TI Factors affecting the specificity and mechanism of action of antisense **oligonucleotide**

AU Agrawal, Sudhir

CS Hybridon, Inc., Milford, MA, 01757, USA

SO Antisense & Nucleic Acid Drug Development (1999), 9(4), 371-375
CODEN: ANADF5; ISSN: 1087-2906

PB Mary Ann Liebert, Inc.

DT Journal; General Review

LA English

AB A review with 58 refs. Progress made in the synthetic chemical of **oligonucleotides** has led to the use of **oligonucleotides** not only as probes and primers but also as therapeutic agents. In antisense therapeutics, short, single-stranded **oligonucleotides** hybridize to mRNA, thereby inhibiting translation of encoded proteins involved in disease. The antisense approach is simple and elegant. The rationale behind antisense therapeutics is simple: to identify an inhibitor of a specific mRNA, one needs to know the **nucleotide** sequence of the mRNA and a complementary **oligonucleotide**. To overcome the nuclease instability of **oligonucleotides**, various analogs have been synthesized in which the **phosphodiester** backbone has been modified. **Phosphorothioate oligodeoxynucleotide** (PS-oligo) is the only modified analog that has shown better activity as an antisense **oligonucleotide** than the **phosphodiester oligonucleotides**. It has become evident that PS-oligos exert biol. activity by multiple mechanisms of action, which can be broadly classified into three categories: (1) sequence-specific antisense activity, (2) sequence-specific non-antisense activity, and (3) non-sequence-specific activity.

RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 39 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:359644 HCAPLUS

DN 131:28622

TI Antisense **oligonucleotides** inhibiting CDK4 expression for growth inhibition and treatment of cancer

IN Morrissey, David; Von Hofe, Eric

PA Hybridon, Inc., USA

SO PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9927087 A1 19990603 WO 1997-US22234 19971121 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,
VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG
AU 9853729 A1 19990615 AU 1998-53729 19971121 <--
PRAI WO 1997-US22234 19971121 <--
AB Disclosed are **oligonucleotides** complementary to CDK4
nucleic acids and methods of regulating the G1 to S phase
transition in a cell and of inhibiting the growth of a cancer cell using
such **oligonucleotides**. Also disclosed are therapeutic compns.
and methods for treating a mammal afflicted with a tumor associated with the
aberrant expression of CDK4 and CDK4-associated proteins such as cyclin D1
and p16.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 40 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:166719 HCAPLUS
DN 130:218274
TI Mdm2-specific antisense **oligonucleotides** for activation of p53
expression and tumor inhibition
IN Chen, Jiandong; Agrawal, Sudhir; Zhang, Ruiwen
PA Hybridon, Inc., USA
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910486	A2	19990304	WO 1998-US17147	19980818 <--
WO 9910486	A3	19991014		
W:				
AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP,				
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,				
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,				
UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:				
GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,				
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2301816	AA	19990304	CA 1998-2301816	19980818 <--
AU 9890237	A1	19990316	AU 1998-90237	19980818 <--
EP 1007658	A2	20000614	EP 1998-942115	19980818 <--
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, FI				
JP 2001513996	T2	20010911	JP 2000-507794	19980818 <--
PRAI US 1997-916384	A	19970822 <--		
US 1998-73567	A	19980506 <--		
WO 1998-US17147	W	19980818 <--		
AB				
The invention provides methods to activate tumor suppressors. The invention further provides antisense oligonucleotides complementary to a portion of the MDM2-encoding RNA and methods for using such antisense oligonucleotides as anal. and diagnostic tools, as potentiators of transgenic animal studies and for gene therapy approaches, and as potential therapeutic agents. The invention also provides methods to augment and synergistically activate a tumor suppressor in conjunction with the use of a DNA-damage inducing agent. Thus, the antisense phosphorothioate oligonucleotide				

5'-tgaaactgaatcctgatcca-3' inhibits mdm2 expression by .apprx.3-5-fold at 100-400 nM concns., causes up to 6.6-fold induction of p21/WAF1 (at 200 nM), activates expression of p53 and thus induces apoptosis and inhibits tumor growth.

L58 ANSWER 41 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:139949 HCAPLUS

DN 130:191877

TI Novel HIV-specific synthetic antisense **oligonucleotides** and methods of their use

IN **Agrawal, Sudhir**

PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9909154	A2	19990225	WO 1998-US16345	19980805 <--
	WO 9909154	A3	19990506		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2300352	AA	19990225	CA 1998-2300352	19980805 <--
	AU 9887713	A1	19990308	AU 1998-87713	19980805 <--
	EP 1007657	A2	20000614	EP 1998-939243	19980805 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2001514884	T2	20010918	JP 2000-509820	19980805 <--
	US 2002168340	A1	20021114	US 2001-837806	20010418 <--
	US 2003100521	A1	20030529	US 2001-896692	20010629 <--
PRAI	US 1997-914827	A	19970819 <--		
	WO 1998-US16345	W	19980805 <--		

AB Disclosed are synthetic **oligonucleotides** having a **nucleotide** sequence specifically complementary to **nucleotides** 324-345 of a conserved gag region of the HIV-1 genome, the **oligonucleotide** consisting of 21 **nucleotides** which are linked via **phosphorothioate internucleotide** linkages and optionally containing 5'- and 3'-terminal 2'-O-**methylribonucleotide** residues. Also disclosed are methods for inhibiting and treating HIV-1 and HIV-2 infection. To determine the preclin. range of anti-HIV activity of various **oligonucleotides**, evaluations were performed against a variety of wild-type and drug-resistant strains of HIV-1, including both laboratory derived and low passage, clin. strains of virus and T-lymphocyte-tropic and monocyte-macrophage-tropic viruses. The **oligonucleotides** remained active against viruses resistant to nevirapine, 3TC and protease inhibitors, but were less active against viruses with mutations conferring resistance to AZT. High test concns. exhibited no toxicity even after 14 days, and the **oligonucleotides** are i.v. and orally bioavailable to rats and monkeys after a single dose. The **phosphorothioated oligonucleotide** 5'-ucgcacccatctctctccuuc-3' (with the four 5' and the four 3' residues comprising 2'-O-**methylribonucleotides**) inhibits viral infection or post-viral adsorption with IC50 = 410 nM and IC90 = 1737 nM.

L58 ANSWER 42 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:76088 HCAPLUS
 DN 130:246352
 TI Cellular distribution of **phosphorothioate oligonucleotide** following intravenous administration in mice
 AU Zhao, Qiuyan; Zhou, Renzhi; Temsamani, Jamal; Zhang, Zhiwei; Roskey, Allysen; Agrawal, Sudhir
 CS Hybridon, Inc., Cambridge, MA, 02139, USA
 SO Antisense & Nucleic Acid Drug Development (1998), 8(6), 451-458
 CODEN: ANADF5; ISSN: 1087-2906
 PB Mary Ann Liebert, Inc.
 DT Journal
 LA English
 AB **Oligonucleotides** are promising therapeutic agents for the prevention or treatment of a variety of diseases. The therapeutic potential of **oligonucleotide** therapy depends greatly on the bioavailability of **oligonucleotides** to their target cells and organs. We previously reported the pharmacokinetics and distribution of **phosphorothioate oligonucleotide** in mice using [35S]-labeled **oligonucleotide** ([35S]-oligo). To extend this study, we administered 30 mg/kg of fluorescent-labeled **oligonucleotide** (FITC-oligo) to mice and examined **oligonucleotide** distribution by measuring the fluorescence intensity in various cells and tissues using flow cytometry. Following FITC-oligo administration, fluorescence was detected in all the tissues examined. In terms of the fluorescent intensity, accumulation was greatest in liver and kidney, intermediate in spleen and bone marrow, and very low in peripheral blood mononuclear cells (PBMC). At 4 h after administration, the level of **oligonucleotide** uptake in PBMC, spleen lymphocytes, and bone marrow cells revealed the following pattern: monocytes/macrophages > B cells > T cells. Confocal microscopy detected intracellular fluorescence in PBMC prepared under the same conditions as those for flow cytometry. These studies provide a rationale for designing cell targets for antisense therapeutics.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 43 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:26511 HCAPLUS
 DN 130:231953
 TI Sequence-specific RNase H cleavage of gag mRNA from HIV-1 infected cells by an antisense **oligonucleotide** in vitro
 AU Veal, Gareth J.; Agrawal, Sudhir; Byrn, Randal A.
 CS Divisions of Hematology, Oncology and Experimental Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 02215, USA
 SO Nucleic Acids Research (1998), 26(24), 5670-5675
 CODEN: NARHAD; ISSN: 0305-1048
 PB Oxford University Press
 DT Journal
 LA English
 AB We have used a RNase protection assay to investigate RNase H cleavage of HIV-1 mRNA mediated by **phosphorothioate antisense oligonucleotides** complementary to the gag region of the HIV-1 genome in vitro. Cell lysate expts. in H9 and U937 cells chronically infected with HIV-1 IIIB showed RNase H cleavage of unspliced gag message but no cleavage of spliced message which did not contain the target gag region. RNase H cleavage products were detected at **oligonucleotide** concns. as low as 0.01 μ M and the RNase H activity was seen to be concentration dependent. Similar expts. with 1-, 3- and 5-mismatch **oligonucleotides** demonstrated sequence specificity at low concns., with cleavage of gag mRNA correlating with the predicted activities of the parent and mismatch **oligonucleotides** based on their hybridization melting temps. Expts. in living cells suggested that

RNase H-specific antisense activity was largely determined by the amount of **oligonucleotide** taken up by the different cell lines studied. RNase H cleavage products were detected in antisense **oligonucleotide** treated MT-4 cells acutely infected with HIV-1 IIIIB, but not in infected H9 cells treated with **oligonucleotide** under the same conditions. The data presented demonstrate potent and specific RNase H cleavage of HIV-1 mRNA mediated by an antisense **oligonucleotide** targeted to HIV-1 gag mRNA, and are in agreement with previous reports that the major obstacle to demonstrating antisense activity in living cells remains the lack of penetration of these agents into the desired cellular compartment.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 44 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:1288 HCAPLUS
DN 130:204679
TI Mixed-backbone **oligonucleotides** as second-generation antisense agents with reduced **phosphorothioate**-related side effects
AU Zhou, Wenqiang; Agrawal, Sudhir
CS Hybridon Inc., Milford, MA, 01757, USA
SO Bioorganic & Medicinal Chemistry Letters (1998), 8(22), 3269-3274
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Mixed-backbone **oligonucleotides** containing alternative **phosphorothioate** and **phosphodiester** linkages in the 2'-O-methylribonucleosides segment show increased affinity with complementary targets, increased stability towards nucleases in vitro and in vivo, and reduced **phosphorothioate**-related prolongation of partial thromboplastin time compared to **phosphorothioate oligodeoxynucleotides**, thereby providing antisense agents with reduced side effects.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 45 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:728545 HCAPLUS
DN 129:339867
TI **Oligonucleotides** mediating specific cytokine induction and their use in vivo in protection from infection
IN Agrawal, Sudhir; Zhao, Qiuyan
PA Hybridon, Inc., USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849288	A1	19981105	WO 1998-US8751	19980430 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 6426334	B1	20020730	US 1997-848229	19970430 <--
AU 9871712	A1	19981124	AU 1998-71712	19980430 <--

EP 991755 A1 20000412 EP 1998-918873 19980430 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 JP 2002505666 T2 20020219 JP 1998-547395 19980430 <--
 EP 1408110 A2 20040414 EP 2004-457 19980430 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY
 US 2002151518 A1 20021017 US 2002-167825 20020612 <--
 PRAI US 1997-848229 A 19970430 <--
 EP 1998-918873 A3 19980430 <--
 WO 1998-US8751 W 19980430 <--
 AB Methods for modulating the synthesis of specific cell-mediated
 immunity-inducing cytokines in vivo using **oligonucleotides** with
 specific structural motifs are described. These methods induce synthesis
 of the cytokines IL-6, IL-12 MIP-1 β and MCP without substantially
 inducing undesired cytokines. The **oligonucleotides** have a
 central CpG **dinucleotide** and are flanked by four domains of 0-50
 bases with at least one of them containing the **tetranucleotide**
 GpGpGpG. Mice were injected i.p. with the **phosphorothioate**
oligonucleotide 5'-TCCATGACGTTCTGATGCTTTTGGGGG-3' at 5-25 mg/kg
 on each of four successive days. On the second day they were infected
 with a LD of murine cytomegalovirus. At low dosages of the
oligonucleotide mean-time-to-death was increased and at
 intermediate dosages the frequency of survival was increased over
 controls. The highest dosage actually had deleterious effects.
 RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 46 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STM

AN 1998:728544 HCAPLUS

DN 129:339865

TI Antisense **oligonucleotides** specific for thymidylate synthase for
 use as an adjunct to **nucleoside** antimetabolite chemotherapy

IN Schmitz, John C.; Agrawal, Sudhir; Chu, Edward

PA Hybridon, Inc., USA

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

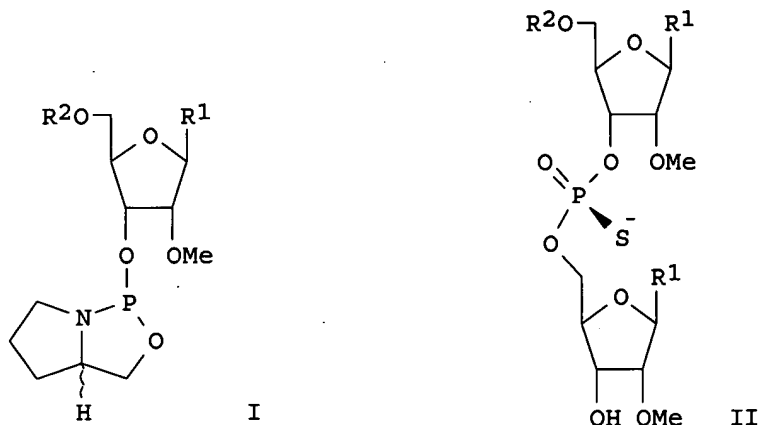
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9849287	A2	19981105	WO 1998-US8722	19980430 <--
	WO 9849287	A3	19990204		
	W:		AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
	AU 9873649	A1	19981124	AU 1998-73649	19980430 <--
PRAI	US 1997-45230P	P	19970430 <--		
	WO 1998-US8722	W	19980430 <--		
AB	Antisense oligonucleotides inhibiting expression of the thymidylate synthase gene are described for use in support of chemotherapy with 5-fluorouracil. Inhibition of thymidylate synthase formation prevents the development of resistance to the 5-fluorouracil in tumors. Phosphoramidate oligonucleotides complementary to a region around the translation start site were synthesized by standard chemical These oligonucleotides inhibited in vitro translation of the synthase mRNA. They also inhibited growth of the breast cancer-derived cell line				

MCF-7 in vitro when delivered in liposomes.

L58 ANSWER 47 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:692676 HCAPLUS
DN 130:133445
TI Pharmacokinetics of **oligonucleotides**
AU **Agrawal, Sudhir**; Zhang, Ruiwen
CS **Hybridon Inc., Cambridge, MA, 02139, USA**
SO Ciba Foundation Symposium (1997), 209(Oligonucleotides as
Therapeutic Agents), 60-78
CODEN: CIBSB4; ISSN: 0300-5208
PB John Wiley & Sons Ltd.
DT Journal; General Review
LA English
AB A review with many refs. The effectiveness of antisense
oligonucleotides as therapeutic agents depends on their
pharmacokinetics, tissue disposition, stability, elimination and safety
profile. Pharmacokinetic data allow one to determine the frequency of
administration and any potential toxicity associated with chronic
administration. **Phosphorothioate oligonucleotides**
degrade from the 3' end, the 5' end, and both the 3' and 5' ends in a
time- and tissue-dependent manner. After i.v. administration in mice,
rats and monkeys, **phosphorothioate oligonucleotides**
are detected in plasma; they distribute rapidly and are retained in the
majority of tissues. The major route of elimination is the urine. The
pharmacokinetic profile is similar following s.c., intradermal or i.p.
administration, but with lower maximum plasma concns.
Phosphorothioate oligonucleotides have a short plasma
half-life in humans. End-modified, mixed-backbone
oligonucleotides (MBOs) contain nuclease-resistant 2'-O-
alkylribonucleotides or **methylphosphonate**
internucleotide linkages at both the 3' and 5' ends of
phosphorothioate oligonucleotides. These end-modified
MBOs have pharmacokinetic profiles similar to those of the parent
phosphorothioate oligonucleotides, but they are
significantly more stable in vivo and they can be administered orally.
Centrally modified MBOs contain modified RNA or DNA in the center of a
phosphorothioate oligonucleotide. They show controlled
degradation and elimination following administration in rats. The
pharmacokinetics of antisense **oligonucleotides** depends on the
sequence, the nature of the **oligonucleotide** linkages and the
secondary structure.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 48 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:660077 HCAPLUS
DN 129:330956
TI Solid-phase stereoselective synthesis of 2'-O-methyl-oligo-ribonucleoside
phosphorothioates using nucleoside bicyclic oxazaphospholidines
AU Guo, MaoJun; Yu, Dong; Iyer, Radhakrishnan P.; **Agrawal,**
Sudhir
CS **Hybridon Inc., Cambridge, MA, 02139, USA**
SO Bioorganic & Medicinal Chemistry Letters (1998), 8(18), 2539-2544
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



AB The use of 2'-OMe-ribonucleoside bicyclic oxazaphospholidines I (R1 = uracil, N-benzoyladenine, N-benzoylcytosine, N-pent-4-enoylguanine; R2 = dimethoxytrityl) derived from (R)- or (S)-2-pyrrolidinemethanol has enabled the stereoselective synthesis of (Rp)-, and (Sp)-2'-O-methyloligoribonucleoside phosphorothioates II (R1 = uracil, N-benzoyladenine, N-benzoylcytosine, N-pent-4-enoylguanine; R2 = dimethoxytrityl). Interestingly, higher stereoselectivity (96-98%) was observed in the synthesis of (Sp)-2'-O-methyl-oligoribonucleoside phosphorothioates compared to that in the case of (Sp)-oligodeoxyribonucleoside phosphorothioates (90%).

IT 215191-10-9DP, controlled pore glass bound

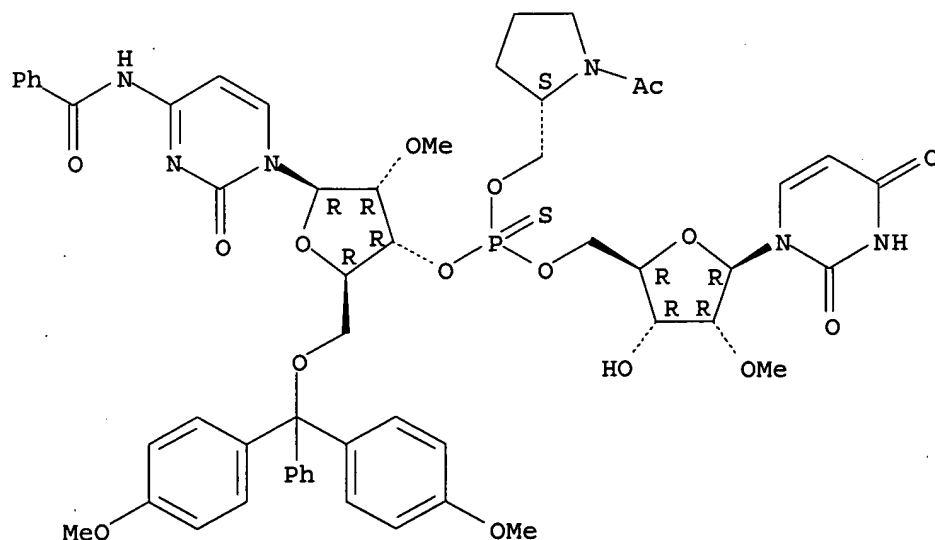
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(solid-phase stereoselective synthesis of 2-O-methyloligoribonucleoside phosphorothioates using nucleoside bicyclic oxazaphospholidines)

RN 215191-10-9 HCAPLUS

CN Uridine, P(O)-[[[(2S)-1-acetyl-2-pyrrolidinyl]methyl]-N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 215191-16-5P 215191-17-6P

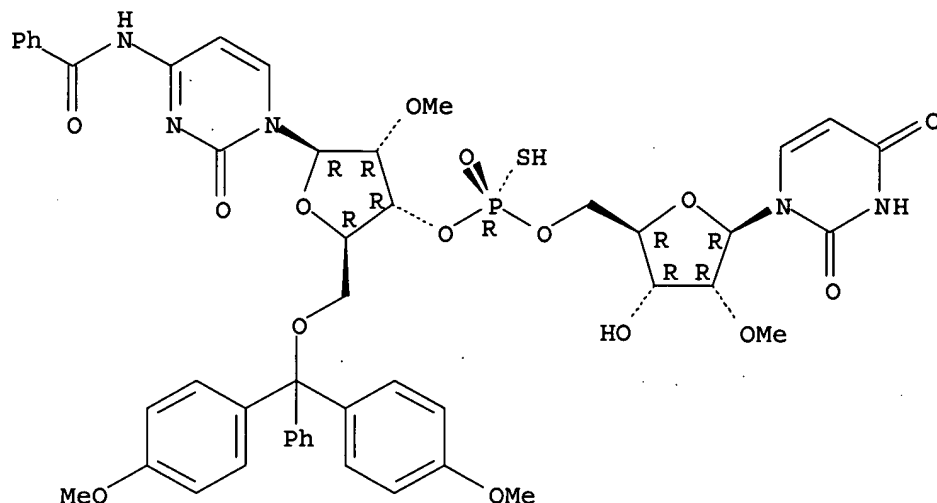
RL: SPN (Synthetic preparation); PREP (Preparation)

(solid-phase stereoselective synthesis of 2-O-methyloligoribonucleoside phosphorothioates using nucleoside bicyclic oxazaphospholidines)

RN 215191-16-5 HCAPLUS

CN Uridine, [P(R)]-N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

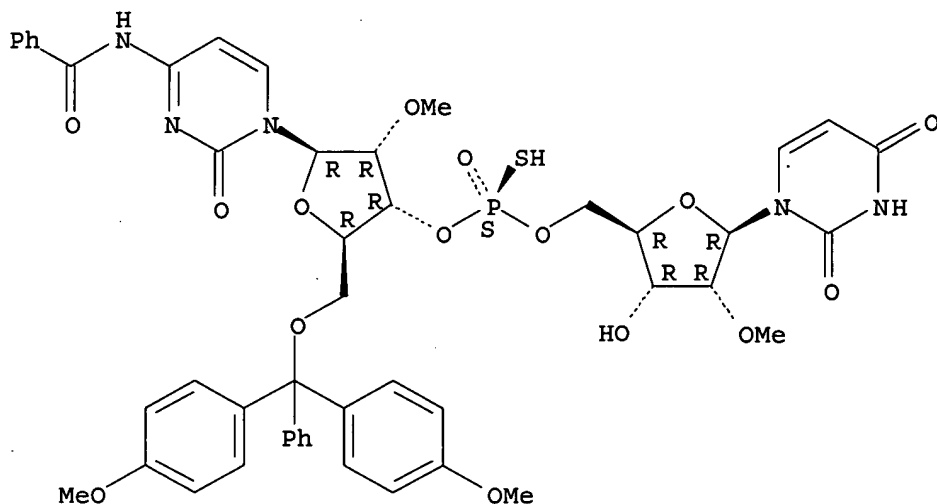
Absolute stereochemistry.



RN 215191-17-6 HCAPLUS

CN Uridine, [P(S)]-N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-P-thiocytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 49 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:621341 HCAPLUS

DN 129:240853

TI Method for sequencing of modified nucleic acids using
electrospray ionization-Fourier transform mass spectrometry

IN Wang, Bing H.

PA Hybridon, Inc., USA
 SO PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840520	A1	19980917	WO 1998-US4919	19980312 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

	AU 9865534	A1	19980929	AU 1998-65534	19980312 <--
PRAI	US 1997-40717P	P	19970314 <--		
	WO 1998-US4919	W	19980312 <--		

AB The invention provides an anal. method for determining the **nucleotide** sequence of **nucleic** acid analytes, including chemical modified **oligonucleotides**. This new method utilizes electrospray ionization-Fourier transform mass spectrometry.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 50 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:621103 HCAPLUS

DN 129:265463

TI Down-regulation of gene expression by colorectal administration of synthetic **oligonucleotides**

IN Zhang, Ruiwen; Agrawal, Sudhir

PA Hybridon, Inc., USA

SO PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840058	A2	19980917	WO 1998-US4914	19980312 <--
	WO 9840058	A3	19981119		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9865533	A1	19980929	AU 1998-65533	19980312 <--
	EP 1007098	A2	20000614	EP 1998-911615	19980312 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2001527536	T2	20011225	JP 1998-539823	19980312 <--
PRAI	US 1997-40738P	P	19970312 <--		
	US 1997-846417	A	19970430 <--		
	WO 1998-US4914	W	19980312 <--		

AB Disclosed is a method of down-regulating the expression of a gene in an animal, wherein an **oligonucleotide** complementary to the gene is colorectally administered to an animal. Also disclosed is a method for introducing an intact **oligonucleotide** into a mammal by

colorectal administration, whereby the **oligonucleotide** is present in intact form in the systemic plasma of the mammal at least four hours following administration.

L58 ANSWER 51 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:606875 HCAPLUS
 DN 129:325906
 TI Effects of **phosphorothioate oligodeoxyribonucleotide**
 and **oligoribonucleotides** on human complement and coagulation
 AU **Kandimalla, Ekambar R.; Shaw, Denise R.; Agrawal, Sudhir**
 CS **Hybridon, Inc, Cambridge, MA, 02139, USA**
 SO **Bioorganic & Medicinal Chemistry Letters (1998), 8(16),**
 2103-2108
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 AB The authors have synthesized and studied the effects of
phosphorothioate (PS) oligodeoxyribonucleotide (DNA) and
oligoribonucleotides (RNA, 2'-O-methyl-RNA and 2'-5'-RNA) on
 complement activation and prolongation of activated partial thromboplastin
 time (aPTT) in vitro. These results suggest that a PS-DNA prolongs aPTT,
 and inhibits complement lysis more than do the PS-RNA analogs.
 RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 52 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:604995 HCAPLUS
 DN 129:200458
 TI **Oligonucleotides** inhibiting expression of the marORAB operon and
 the control of multiple antibiotic resistance in bacteria
 IN Levy, Stuart B.; Von Hofe, Eric
 PA **Hybridon, Inc., USA; Trustees of Tufts College**
 SO **PCT Int. Appl., 44 pp.**
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837188	A1	19980827	WO 1998-US2999	19980220 <--
	W:				
	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK,				
	EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP,				
	KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,				
	NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,				
	UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,				
	FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,				
	GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9863284	A1	19980909	AU 1998-63284	19980220 <--
	US 6136602	A	20001024	US 1998-27130	19980220 <--
	JP 2001512324	T2	20010821	JP 1998-536777	19980220 <--
	US 6485973	B1	20021126	US 2000-596390	20000616 <--
	US 2003032612	A1	20030213	US 2002-153275	20020521 <--
PRAI	US 1997-38663P	P	19970221	<--	
	US 1998-27130	A1	19980220	<--	
	WO 1998-US2999	W	19980220	<--	
	US 2000-596390	B1	20000616	<--	
AB	Antisense oligonucleotides inhibiting translation of the transcript of the marORAB operon of Escherichia coli and related Enterobacteria and that can be used in the control of multiple antibiotic resistance is described. These oligonucleotides may be used therapeutically in the treatment of multiple antibiotic resistant				

infections. **Phosphorothioate oligonucleotides** targeted to the marA gene were shown to inhibit expression of a marA/lacZ gene fusion in a dose-dependent manner. When used in combination with norfloxacin, these **oligonucleotides** enhanced the killing effect of the antibiotic.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 53 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:567887 HCAPLUS
DN 129:299001
TI Study of **phosphorothioate**-modified **oligonucleotide** resistance to 3'-exonuclease using capillary electrophoresis
AU Gilar, Martin; Belenky, Alexei; Budman, Yeva; Smisek, David L.; Cohen, Aharon S.
CS Hybridon, Inc., 620 Memorial Drive, Cambridge, MA, 02139, USA
SO Journal of Chromatography, B: Biomedical Sciences and Applications (1998), 714(1), 13-20
CODEN: JCBEBP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
AB The effect of **phosphorothioate** (PS) **internucleotide** linkages on the stability of **phosphodiester oligodeoxyribonucleotides** (ODNs) was investigated using 25-mer ODNs containing single or multiple PS backbone modifications. The in vitro stability of the oligomers was measured both in 3'-exonuclease solution and in plasma. For the separation of ODNs, capillary electrophoresis with a replaceable polymer separation matrix was used. As expected, DNA fragments with PS linkages at the 3'-end were found to be more resistant to 3'-exonuclease hydrolysis. Also increasing exonuclease resistance was the non-specific adsorption of **phosphorothioate** ODNs to enzyme.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 54 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:427126 HCAPLUS
DN 129:183710
TI Safety and tolerance of **phosphorothioates** in humans
AU Schechter, P. J.; Martin, R. R.
CS Drug Development, Hybridon, Inc., Cambridge, MA, 02139, USA
SO Handbook of Experimental Pharmacology (1998), 131(Antisense Research and Application), 233-241
CODEN: HEPHD2; ISSN: 0171-2004
PB Springer-Verlag
DT Journal; General Review
LA English
AB A review with many refs. on the toxicity of **phosphorothioate oligonucleotides** in humans emphasizing GEM 91. Although there is limited experience, it is clear that **phosphorothioate oligonucleotides** can be used over a wide range of doses and for a duration of at least several weeks with good safety. This tolerance profile should allow clin. proof of the concepts for systemic antisense therapeutics and potential wide use in a variety of clin. conditions.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 55 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:344499 HCAPLUS
DN 129:23425
TI Reversal of drug resistance through **oligonucleotides** complementary to the Plasmodium falciparum-specific pfmdr1 gene region
IN Baker, Robert H., Jr.; Rapaport, Eliezer; Zamecnik, Paul C.

PA **Hybridon, Inc., USA; Worcester Foundation for Biomedical Research**

SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9821323	A2	19980522	WO 1997-US20590	19971112 <--
	WO 9821323	A3	19981126		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 6440660	B1	20020827	US 1996-745485	19961112 <--
	AU 9854348	A1	19980603	AU 1998-54348	19971112 <--
PRAI	US 1996-745485	A	19961112	<--	
	US 1995-560474	B1	19951117	<--	
	US 1996-634588	A2	19960418	<--	
	WO 1997-US20590	W	19971112	<--	
AB	<p>The present invention provides methods of resensitizing an anti-drug-resistant infectious agent to a drug. Synthetic oligonucleotides are designed having a nucleotide sequence complementary to to a conserved region, an ATP-binding site, the translational start site, and a Plasmodium falciparum-specific region in the pfmdr1 gene. The oligonucleotides down-regulate the expression of pfmdr1 nucleic acid. In the presence of such oligonucleotides specific for pfmdr1, W2mef, a mefloquine-resistant strain of P. falciparum, becomes significantly more sensitive to mefloquine. This is demonstrated both by reduced total incorporation of [3H]-hypoxanthine, and in the downward shift in the threshold dose at which the parasite loses tolerance to mefloquine. These effects are specific, since mismatch control oligonucleotides do not significantly alter mefloquine sensitivity.</p>				

L58 ANSWER 56 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:292802 HCAPLUS

DN 129:49051

TI In vivo pharmacokinetics of **oligonucleotides**

AU **Agrawal, Sudhir**

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Applied Antisense Oligonucleotide Technology (1998), 365-385.

Editor(s): Stein, C. A.; Kreig, Arthur M. Publisher: Wiley-Liss, New York, N. Y.

CODEN: 65ZQAC

DT Conference; General Review

LA English

AB A review with >30 refs. primarily concerning the in vivo pharmacokinetics of **phosphorothioate oligonucleotides**.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 57 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:230586 HCAPLUS

DN 129:12318

TI Synergistic inhibition of HIV-1 by an antisense **oligonucleotide** and **nucleoside** analog reverse transcriptase inhibitors

AU Veal, Gareth J.; Agrawal, Sudhir; Byrn, Randal A.

CS Beth Israel Deaconess Medical Center, Divisions of Hematology/Oncology and
Experimental Medicine, Harvard Medical School, Boston, MA, 02215, USA

SO Antiviral Research (1998), 38(1), 63-73
CODEN: ARSRDR; ISSN: 0166-3542

PB Elsevier Science B.V.

DT Journal

LA English

AB We have studied the effects of the gag antisense **phosphorothioate oligonucleotide** GEM 91 and mismatch antisense controls on the antiviral activities of ddC and other **nucleoside** analogs in HIV-infected MT-4 cells using a cytoprotection based assay. Under standard assay conditions, i.e. simultaneous incubation of drugs, HIV-1 IIIB and MT-4 cells, both GEM 91 and mismatch controls interacted synergistically with ddC resulting in an approx. 40-fold decrease in the IC50 value of ddC; this suggests a potent but sequence non-specific effect of GEM 91. Under post-adsorption assay conditions, i.e. pre-incubation of virus and cells and removal of excess HIV before drug addition, GEM 91 exhibited synergism with ddC, with an approx. 5-fold decrease in ddC IC50 value. This favorable interaction was not seen with any of the mismatch **oligonucleotides**, suggesting the involvement of a sequence-specific mechanism of action. Similar results were seen with the thymidine analogs AZT and d4T in combination with GEM 91. These data suggest a potential role for GEM 91 and future sequence-specific antisense drugs in combination with **nucleoside** analogs for the treatment of HIV infection. It is essential that potential interactions between new and existing classes of anti-HIV drugs are studied extensively as antiretroviral drug combinations become increasingly more complex.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 58 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:192125 HCAPLUS

DN 128:266272

TI Inhibition of neovascularization using vascular endothelial growth factor-specific **oligonucleotides**

IN Robinson, Gregory S.; Hodgson, Smith Lois Elaine

PA Hybridon, Inc., USA; Children's Medical Center Corp.

SO U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 98,942.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5731294	A	19980324	US 1995-378860	19950126 <--
	US 6410322	B1	20020625	US 1993-98942	19930727 <--
	CA 2167680	AA	19950209	CA 1994-2167680	19940726 <--
	CN 1131437	A	19960918	CN 1994-193482	19940726 <--
	US 5639872	A	19970617	US 1995-398945	19950302 <--
	US 5710136	A	19980120	US 1995-501713	19950712 <--
	US 5801156	A	19980901	US 1995-501626	19950712 <--
	US 5814620	A	19980929	US 1995-501356	19950712 <--
	US 5639736	A	19970617	US 1995-502185	19950713 <--
	US 5661135	A	19970826	US 1995-501779	19950713 <--
	US 5641756	A	19970624	US 1995-569926	19951208 <--
	CA 2210998	AA	19960801	CA 1996-2210998	19960126 <--
	WO 9623065	A2	19960801	WO 1996-US1189	19960126 <--
	WO 9623065	A3	19960926		
	W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,			

IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
NE, SN, TD

AU 9649074 A1 19960814 AU 1996-49074 19960126 <--
AU 712579 B2 19991111
EP 805858 A2 19971112 EP 1996-905270 19960126 <--
EP 805858 B1 20010613

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE

JP 11500426 T2 19990112 JP 1996-523058 19960126 <--
US 6399586 B1 20020604 US 1999-320911 19990527 <--

PRAI US 1993-98942 A2 19930727 <--
US 1995-378860 A2 19950126 <--
US 1995-398945 A3 19950302 <--
US 1995-569926 A2 19951208 <--
WO 1996-US1189 W 19960126 <--
US 1996-629730 B2 19960409 <--
US 1996-761708 A1 19961206 <--
US 1998-124304 B1 19980729 <--

AB Disclosed are methods of reducing neovascularization and of treating various disorders associated with neovascularization. These methods include administering to a tissue or subject a synthetic **oligonucleotide** specific for vascular endothelial growth factor **nucleic acid** effective in inhibiting the expression of vascular endothelial growth factor.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 59 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:184004 HCAPLUS
DN 128:227059
TI Method for using **oligonucleotides** having modified CpG **dinucleosides** to control gene expression
IN Agrawal, Sudhir
PA Hybridon, Inc., USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9811211	A2	19980319	WO 1997-US16017	19970910 <--
	WO 9811211	A3	19980416		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5856462	A	19990105	US 1996-711568	19960910 <--
	AU 9743399	A1	19980402	AU 1997-43399	19970910 <--
	EP 928335	A2	19990714	EP 1997-941505	19970910 <--
	EP 928335	B1	20030402		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2001500511	T2	20010116	JP 1998-513822	19970910 <--
	AT 236248	E	20030415	AT 1997-941505	19970910 <--
	PT 928335	T	20030731	PT 1997-941505	19970910 <--
	ES 2190541	T3	20030801	ES 1997-941505	19970910 <--
	US 2003036516	A1	20030220	US 1998-103745	19980624 <--
PRAI	US 1996-711568	A	19960910 <--		
	WO 1997-US16017	W	19970910 <--		

AB The invention relates to modified **oligonucleotides** that are useful for studies of gene expression and for the antisense therapeutic approach. The invention provides modified **oligonucleotides** that inhibit gene expression and that produce fewer side effects than conventional **phosphorothioate oligonucleotides**. In particular, the invention provides modified CpG-containing **oligonucleotides** that result in reduced splenomegaly and platelet depletion when administered to a mammal, relative to conventional CpG-containing **phosphorothioate oligonucleotides**. The modifications make comprise **alkylphosphonate** CpG, inverted CpG, 2'-O-substituted CpG, 5-methylcytosine CpG, stereospecific **phosphorothioate** CpG, **phosphotriester** CpG, **phosphoramidate** CpG, and 2'-5' CpG. The invention further provides methods for using such **oligonucleotides** to modulate gene expression in vivo, including such use for therapeutic treatment of diseases caused by aberrant gene expression.

L58 ANSWER 60 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:158635 HCAPLUS

DN 128:278614

TI Pharmacokinetics and metabolism of an **oligodeoxynucleotide phosphorothioate** (GEM91) in cynomolgus monkeys following intravenous infusion

AU Grindel, J. Michael; Musick, Timothy J.; Jiang, Jhiwei; Roskey, Allysen; Agrawal, Sudhir

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Antisense & Nucleic Acid Drug Development (1998), 8(1), 43-52

CODEN: ANADF5; ISSN: 1087-2906

PB Mary Ann Liebert, Inc.

DT Journal

LA English

AB The pharmacokinetics and metabolism of an antisense **oligonucleotide phosphorothioate** (GEM91®) were studied in cynomolgus monkeys following i.v. infusion. [35S]-Labeled GEM91 was administered to 12 monkeys by means of a 2-h i.v. infusion at a dose of 4 mg/kg. Plasma pharmacokinetic anal. revealed that the maximum plasma concentration was 41.7

µg equivalent/mL, which was achieved in 2.13 h. The plasma elimination half-life was 55.8 h based on radioactivity levels. Urinary excretion represented the major pathway of elimination, with 70% of the administered dose excreted in urine over 240 h. The **oligonucleotide** was widely distributed to tissues. The highest concns. were observed in the liver and kidney. Anal. of the extracted **oligonucleotide** following post-labeling with [32P] on polyacrylamide gel electrophoresis showed the presence of both intact and degraded **oligonucleotide** in plasma, kidney, liver, spleen, and lymph nodes. Based on the methods used for post-labeling (either 3'-end or 5'-end), different patterns of bands were observed on polyacrylamide gel electrophoresis, suggesting metabolic modification of the administered **oligonucleotide**.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 61 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:158579 HCAPLUS

DN 128:279839

TI Impact of 3'-exonuclease stereoselectivity on the kinetics of **phosphorothioate oligonucleotide** metabolism

AU Gilar, Martin; Belenky, Alexei; Budman, Yeva; Smisek, David L.; Cohen, Aharon S.

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Antisense & Nucleic Acid Drug Development (1998), 8(1), 35-42

CODEN: ANADF5; ISSN: 1087-2906

PB Mary Ann Liebert, Inc.

DT Journal
 LA English
 AB For the enzymic digestion of a 25-mer **phosphorothioate** (PS) **oligonucleotide**, the reaction kinetics was previously determined to be the sum of two parallel processes: a fast and a very slow phase of digestion suggesting a two-exponential model. A characteristic metabolite profile was observed both in vitro and in vivo. This behavior is shown to be the result of the stereoselective cleavage of chiral R-configuration and S-configuration PS **internucleotide** linkages by 3'-exonucleases. The stereoselective nature of 3'-exonuclease action was analyzed by reverse-phase HPLC. The separation of eight diastereomers of the tetramer TTCT (5'-3') was used to follow the stereoselective course of exonuclease hydrolysis of PS **internucleotide** linkages. Degradation of the 25-mer parent compound having a 3' S-terminal **internucleotide** linkage was calculated to be more than 300 times slower than an analog with a 3'-terminal R-configuration. These results support an approach for protecting antisense **oligonucleotides** based on the chirality of only the 3'-end **internucleotide** linkage.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 62 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:89349 HCAPLUS
 DN 128:162876
 TI Antisense **oligonucleotides** and methods for treating specific gene expression-related diseases and disorders in humans
 IN Schechter, Paul J.; Martin, B. Russel; Tournerie, Christophe; Agrawal, Sudhir
 PA Hybridon, Inc., USA
 SO PCT Int. Appl., 93 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9803646	A1	19980129	WO 1996-US12056	19960722 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9665924	A1	19980210	AU 1996-65924	19960722 <--
PRAI	WO 1996-US12056		19960722 <--		

AB The present invention provides therapeutic compns. and methods for treating humans suffering from diseases or disorders caused by cellular expression of aberrant exogenous genes or aberrant endogenous genes comprising administering to the human a therapeutically effective amount of an **oligonucleotide** capable of specifically down-regulating the expression of such a gene. Thus, **oligodeoxyribonucleotides** are provided which are antisense to residues 324-348 of the conserved gag gene region of human immunodeficiency virus type 1 (HIV-1). These antisense **oligonucleotides** are more specific, less toxic, and have greater nuclease resistance than many other chemotherapeutic agents designed to inhibit HIV-1 replication. In addition, they are more active in inhibiting viral replication than other known antisense **oligonucleotides** containing less than the 324-348 HIV-1 gag sequence. The efficacy and pharmacokinetics profile of **phosphorothioated** 5'-ctctcgacccatctctctcttct-3' in the treatment of HIV-1-infected human cell lines are described.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 63 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:30041 HCAPLUS
DN 128:176130
TI Toxicologic effects of an **oligodeoxynucleotide phosphorothioate** and its analogs following intravenous administration in rats
AU Agrawal, Sudhir; Zhao, Qiuyan; Jiang, Zhiwei; Oliver, Carolyn; Giles, Herschel; Heath, James; Serota, David
CS Hybridon, Inc., Cambridge, MA, 02139, USA
SO Antisense & Nucleic Acid Drug Development (1997), 7(6), 575-584
CODEN: ANADF5; ISSN: 1087-2906
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB The aim of the present study is to evaluate the in vivo toxicol. effects of a **phosphorothioate oligodeoxynucleotide** (PS oligo) and three of its analogs [PS oligo containing four **methylphosphonate** linkages at the 3' and 5'-ends (MBO 1), PS oligo containing four 2'-O-**methylribonucleosides** at both the 3'- and 5'-ends (MBO 2), and PS oligo containing an 8 bp loop region at the 3'-end (self-stabilized oligo)]. **Oligodeoxynucleotides** were administered i.v. to male and female rats at doses of 3, 10, and 30 mg/kg/day for 14 days. Rats were killed on day 15, blood samples were collected for hematol. and clin. chemical detns., and tissues, including lymph nodes, spleens, livers, and kidneys, were subjected to pathol. exams. The toxicity profiles of the four **oligodeoxynucleotides** were very similar, but differed in magnitude. In terms of the severity of the abnormalities caused by the **oligodeoxynucleotides**, the order was MBO 2 > PS oligo > self-stabilized oligo > MBO 1. Alterations in hematol. parameters included thrombocytopenia, anemia, and neutropenia. Abnormalities in clin. chemical parameters observed with PS oligo or MBO 2 were dose-dependent elevation of liver transaminases and reduction of the levels of alkaline **phosphatase**, albumin, and total protein. In addition, MBO 2 caused elevation of the total bilirubin level in male rats at the 30 mg/kg dose. No major alterations in hematol. or clin. chemical were observed in rats receiving MBO 1 or self-stabilized oligo. Dose-dependent enlargements of spleen, liver, and kidney were observed, especially in rats receiving PS oligo and MBO 2. Pathol. studies showed a generalized hyperplasia of the reticuloendothelial (RE) system in the tissues examined. Alterations in the spleen were mainly RE cell hyperplasia and hematopoietic cell proliferation. In addition to RE cell hyperplasia, lymph nodes showed necrosis, hepatocytes showed cytol. alterations and necrosis, and kidneys showed renal tubule regeneration. The severity of pathol. changes observed was **oligodeoxynucleotide** dependent, in the order of MBO 2 > PS oligo > self-stabilized oligo > MBO 1.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 64 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:324 HCAPLUS
DN 128:151268
TI HPLC of **oligodeoxyribonucleoside phosphorothioates**
AU Metelev, V. G.; Tashlitskii, V. N.; Agrawal, S.
CS Chem. Fac., Moscow State Univ., Moscow, 119899, Russia
SO Bioorganicheskaya Khimiya (1997), 23(9), 742-746
CODEN: BIKHD7; ISSN: 0132-3423
PB MAIK Nauka
DT Journal
LA Russian

- AB Conditions are described for the separation of synthetic **oligodeoxyribonucleoside phosphorothioates** by HPLC using a weak anion exchanger Wide-Pore PEI and for the separation of **oligodeoxyribonucleotides** with mixed **phosphate** and **phosphorothioate internucleotide** bonds on a Partisphere C18 support in ion-pair conditions. The influence of the **nucleoside** composition and the number of **phosphorothioate** bonds on the retention time was studied.
- L58 ANSWER 65 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:811814 HCAPLUS
DN 128:154339
TI Sequencing of modified **oligonucleotides** using in-source fragmentation and delayed pulsed ion extraction matrix-assisted laser desorption ionization time-of-flight mass spectrometry
AU Wang, Bing H.; Hopkins, Christopher E.; Belenky, Alexei B.; Cohen, Aharon S.
CS Analytical Research, **Hybridon**, Inc., Cambridge, MA, 02139, USA
SO International Journal of Mass Spectrometry and Ion Processes (1997), 169/170, 331-350
CODEN: IJMPDN; ISSN: 0168-1176
PB Elsevier Science B.V.
DT Journal
LA English
AB Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOFMS) was used to sequence modified **oligonucleotides** (MONs). Under delayed pulsed ion extraction conditions, sequence ions of MONs resulting from fragmentation within the ion source can be observed. In this work, several common types of antisense MONs with sizes up to 25-mer were studied including an **oligodeoxynucleotide** (ODN) of **phosphorothioate-phosphodiester** (PS-PO) chimera, an all PS ODN, a partially 2'-O-methylated all PS **oligodeoxyribonucleotide-oligoribonucleotide** (ODN-ON) chimera, and an ODN of **phosphorothioate-methylphosphonate** (PS-MP) chimera. The sequence ions observed include 'w', 'd', as well as hitherto little discussed 'a' and 'z' ions. While a complete sequence can be constructed from 'w' ions for chimeric PS-PO ODN, all PS ODN, and chimeric PS ODN-ON, 'a' ions or 'd' ions provide useful supplemental information. For the PS-MP ODN, however, 'd' ions are critical in filling the gap in the sequence constructed from 'w' ions. The method provides a rapid quality control tool in **oligonucleotide** synthesis allowing sequence verification to be accomplished in minutes rather than hours needed by chemical or enzymic methods. The observation that the fragmentation pattern in the PS ON region is rather similar to that of PS ODN together with the observation of 'a' ions suggests that backbone cleavage pathways may not always involve **nucleobases** losses. Fragmentation mechanisms alternative to those found in MALDI-TOFMS literature have been proposed.
- RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L58 ANSWER 66 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:709133 HCAPLUS
DN 128:60530
TI Pattern and kinetics of cytokine production following administration of **phosphorothioate oligonucleotides** in mice
AU Zhao, Qiyuan; Temsamani, Jamal; Zhou, Ren-Zhi; **Agrawal, Sudhir**
CS **Hybridon Inc., Cambridge, MA, 02139, USA**
SO Antisense & Nucleic Acid Drug Development (1997), 7(5), 495-502
CODEN: ANADF5; ISSN: 1087-2906
PB Liebert
DT Journal
LA English

AB **Phosphorothioate oligonucleotides** with certain sequences or structure motifs can stimulate the immune system. We administered to mice a 27-mer **phosphorothioate oligonucleotide** (sequence 5'-TCG TCG CTG TCT CCG CTT CTT CTT GCC-3'), which has previously been shown to cause splenomegaly and hypergammaglobulinemia on in vivo administration in mice, and studied the pattern and kinetics of cytokine production at both the splenic mRNA and serum protein levels. Following i.p. administration of 50 mg/kg of **oligonucleotide**, significant increases in the splenic mRNA levels of IL-6, IL-12p40, IL-1 β , and IL-1Ra and serum levels of IL-6, IL-12, MIP-1 β , and MCP-1 were observed. In contrast, no significant differences in splenic mRNA levels of IL-2, IL-4, IL-5, IL-9, IL-13, IL-15, IFN- γ , or MIF or serum levels of IL-2, IL-4, IL-5, IL-10, IFN- γ , or GM-CSF were detected. The induction of IL-12 secretion was dependent on the sequence and dose of the **oligonucleotides**. One **oligonucleotide** (sequence 5'-GAG AAC GCT CGA CCT TCG AT-3') induced a high level of IL-12 secretion even at 5 mg/kg, whereas another **oligonucleotide** (sequence 5'-CTC TGC CAC CCA TCT CTC TCC TTC T-3') did not induce significant IL-12 secretion even at 50 mg/kg. IL-12 secretion induced by various doses of **oligonucleotide** has the same kinetics but differs in magnitude. These studies show a distinct pattern and kinetics of cytokine production following **oligonucleotide** administration and further demonstrate that cytokine induction is not a general property of **phosphorothioate oligonucleotides** but is dependent on the sequence and dose of the **oligonucleotides**.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 67 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:641664 HCAPLUS

DN 127:327338

TI Kinetics of **phosphorothioate oligonucleotide** metabolism in biological fluids

AU Gilar, M.; Belenky, A.; Smisek, D. L.; Bourque, A.; Cohen, A. S.

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Nucleic Acids Research (1997), 25(18), 3615-3620

CODEN: NARHAD; ISSN: 0305-1048

PB Oxford University Press

DT Journal

LA English

AB The in vitro stability and metabolism of GEM91, a 25mer **phosphorothioate antisense oligonucleotide** complementary to the gag mRNA region of HIV-1, was investigated using capillary electrophoresis (CE). The in vitro degradation of the parent compound at 37°C was followed over the course of 120 h in human plasma. A CE method using laser-induced fluorescence detection was able to detect 5'-end intact metabolites including the parent compound extracted from biol. fluids. Because the primary metabolic pathway is believed to be via 3'-exonuclease activity, the results of this study were compared with the stability of the compound in a solution containing 3'-exonuclease. The numerical

solution of sequential first-order reactions was used to obtain kinetic parameters. Exonuclease digestion of the parent compound, as measured using an automated CE-UV instrument, yielded striking similarities between the two in vitro systems as well as between in vitro and in vivo systems.

L58 ANSWER 68 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:520014 HCAPLUS

DN 127:170932

TI Pharmacokinetics of **phosphorothioate oligonucleotides** and their novel analogs

AU Agrawal, Sudhir; Zhang, Ruiwen

CS Hydridon, Inc., Cambridge, MA, USA
 SO Antisense Oligodeoxynucleotides and Antisense RNA (1997), 57-78.
 Editor(s): Weiss, Benjamin. Publisher: CRC, Boca Raton, Fla.
 CODEN: 64UKAU
 DT Conference; General Review
 LA English
 AB A review, with 34 refs. The authors summarize their recent work on the pharmacokinetics of a **phosphorothioate oligonucleotide** and analogs following i.v. dosing in rats to illustrate the role of chemical modifications on the improvement of pharmacokinetics of antisense **oligonucleotides**. Initial studies examining oral bioavailability of antisense **oligonucleotides** are also reviewed.

L58 ANSWER 69 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:425975 HCAPLUS

DN 127:131000

TI Modified vascular endothelial growth factor (VEGF)-specific **oligonucleotides**

IN Robinson, Gregory S.

PA **Hybridon, Inc., USA**

SO U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 398,945.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5641756	A	19970624	US 1995-569926	19951208	<--
	US 6410322	B1	20020625	US 1993-98942	19930727	<--
	US 5731294	A	19980324	US 1995-378860	19950126	<--
	US 5639872	A	19970617	US 1995-398945	19950302	<--
	CA 2214431	AA	19960906	CA 1996-2214431	19960229	<--
	WO 9627006	A2	19960906	WO 1996-US2840	19960229	<--
	WO 9627006	A3	19961017			
	W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	AU 9651791	A1	19960918	AU 1996-51791	19960229	<--
	EP 815218	A2	19980107	EP 1996-908608	19960229	<--
	EP 815218	B1	20040421			
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 11501508	T2	19990209	JP 1996-526431	19960229	<--
	AT 264912	E	20040515	AT 1996-908608	19960229	<--
	CA 2239991	AA	19970619	CA 1996-2239991	19961205	<--
	WO 9721808	A1	19970619	WO 1996-US19320	19961205	<--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9712793	A1	19970703	AU 1997-12793	19961205	<--
	EP 865489	A1	19980923	EP 1996-943587	19961205	<--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000501941	T2	20000222	JP 1997-522098	19961205	<--
	WO 9720925	A1	19970612	WO 1996-US20441	19961206	<--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
 LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,
 RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
 MR, NE, SN, TD, TG

AU 9716869	A1	19970627	AU 1997-16869	19961206 <--
US 6306829	B1	20011023	US 1996-761708	19961206 <--
US 6649596	B1	20031118	US 1998-124304	19980729 <--
US 6399586	B1	20020604	US 1999-320911	19990527 <--
PRAI US 1993-98942	A2	19930727	<--	
US 1995-378860	A2	19950126	<--	
US 1995-398945	A2	19950302	<--	
US 1995-569926	A	19951208	<--	
WO 1996-US2840	W	19960229	<--	
US 1996-629730	A	19960409	<--	
WO 1996-US19320	W	19961205	<--	
US 1996-761708	A1	19961206	<--	
WO 1996-US20441	W	19961206	<--	
US 1998-124304	B1	19980729	<--	

AB Disclosed are **oligonucleotides** complementary to VEGF-specific **nucleic acids** useful in reducing the expression of VEGF. Also disclosed are pharmaceutical formulations containing such **oligonucleotides** useful for treating various disorders associated with neovascularization and angiogenesis.

L58 ANSWER 70 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:411729 HCAPLUS

DN 127:144688

TI In vivo pharmacokinetics of **phosphorothioate oligonucleotides** containing contiguous guanosines

AU Agrawal, Sudhir; Tan, Weitian; Cai, Quiyin; Xie, Xiaowei; Zhang, Ruiwen

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Antisense & Nucleic Acid Drug Development (1997), 7(3), 245-249

CODEN: ANADF5; ISSN: 1087-2906

PB Liebert

DT Journal

LA English

AB To carry out in vivo pharmacokinetic studies, three 29-mer **phosphorothioate oligonucleotides** were synthesized with a common 25-mer sequence but differing in 4 addnl. **nucleotides**, containing either 4 contiguous guanosines at the 5'-end, 4 guanosines at the 3'-end, or GTGT at the 3'-end. The first 2 oligomers may form hyperstructures, whereas the third oligomer is a control sequence and does not contain contiguous guanosines. A dose of 10 mg/kg of [35S]-labeled **phosphorothioate oligonucleotide** was administered i.v. to male Sprague-Dawley rats. In vivo stability, plasma clearance, tissue distribution, and elimination of the **oligonucleotides** were sequence dependent, especially if sequences have the ability to form certain secondary structures or hyperstructures.

L58 ANSWER 71 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:411351 HCAPLUS

DN 127:118231

TI In vivo metabolic profile of a **phosphorothioate oligodeoxyribonucleotide**

AU Temsamani, Jamal; Roskey, Allysen; Chaix, Carole; Agrawal, Sudhir

CS Hybridon, Inc., Cambridge, MA, 02139, USA

SO Antisense & Nucleic Acid Drug Development (1997), 7(3), 159-165

CODEN: ANADF5; ISSN: 1087-2906

PB Liebert

DT Journal
 LA English
 AB Antisense **phosphorothioate oligodeoxyribonucleotides** (PS **oligonucleotides**) have the ability to inhibit individual gene expression in the potential treatment of cancer and viral diseases. Following administration in vivo, PS **oligonucleotides** are rapidly cleared from the plasma and distributed to various organs. However, the manner in which administered **oligonucleotides** are metabolized in plasma and tissues is poorly understood. In this study, a 25-mer PS **oligonucleotide** (GEM®91) complementary to the gag gene mRNA of the human immunodeficiency virus (HIV-1) was administered to mice through i.v. injections to investigate its metabolism. The PS **oligonucleotide** was extracted from plasma at 1 h postadministration and from kidney and liver at 24 h postadministration. After extraction, the PS **oligonucleotide** and its metabolites were tailed with dA and annealed to a dT-tailed plasmid. The recombinant plasmid was ligated and used to transform competent bacteria. The region of interest containing the PS **oligonucleotide** was then sequenced. Our results show that degradation of the PS **oligonucleotide** in plasma was primarily from the 3'-end. However, in kidney and liver, degradation was primarily from the 3'-end, but a large proportion of the PS **oligonucleotide** was degraded from the 5'-end as well. We also studied the metabolism of PS **oligonucleotide** in plasma after 2-h i.v. infusion in HIV-infected patients. The degradation of the PS **oligonucleotide** in plasma was primarily from the 3'-end. This study is important in understanding the metabolism of antisense PS **oligonucleotide** in vivo in general but also provides guidance for designing second-generation antisense **oligonucleotides** with improved stability and safety profile.

L58 ANSWER 72 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:303410 HCAPLUS
 DN 126:288115
 TI Inverted chimeric and hybrid **oligonucleotides** for antisense therapy and studies of gene expression
 IN Agrawal, Sudhir
 PA Hybridon Inc., USA
 SO PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9706662	A2	19970227	WO 1996-US13371	19960816	<--
	W: AU, BG, BR, CA, CN, HU, IL, JP, LV, NO, NZ, PL, RO, SI, UA					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, IE, IT, LU, NL, PT, SE					
	US 5652356	A	19970729	US 1995-516454	19950817	<--
	CA 2229811	AA	19970227	CA 1996-2229811	19960816	<--
	AU 9669538	A1	19970312	AU 1996-69538	19960816	<--
	JP 11512088	T2	19991019	JP 1996-509535	19960816	<--
	EP 1019428	A2	20000719	EP 1996-930536	19960816	<--
	EP 1019428	B1	20030625			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	AT 243706	E	20030715	AT 1996-930536	19960816	<--
	EP 1340765	A2	20030903	EP 2003-10207	19960816	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	PT 1019428	T	20031031	PT 1996-930536	19960816	<--
	ES 2201198	T3	20040316	ES 1996-930536	19960816	<--
	US 5773601	A	19980630	US 1997-886860	19970701	<--
	US 5973136	A	19991026	US 1997-886670	19970701	<--
PRAI	US 1995-516454	A	19950817			<--

EP 1996-930536 A3 19960816 <--
 WO 1996-US13371 W 19960816 <--

AB Modified **oligonucleotides** are disclosed that are useful for studies of gene expression and for the antisense therapeutic approach. The invention provides inverted hybrid **oligonucleotides** and inverted chimeric **oligonucleotides**, both of which produce reduced side effects, relative to traditional **phosphorothioate**, hybrid or chimeric **oligonucleotides**. The inverted hybrid and inverted chimeric **oligonucleotides** showed reduced complement activation, reduced mitogenicity, and reduced inhibition of clotting in vitro. The effect of the **oligonucleotides** of the invention on RNase H activity and on melting temperature is also reported.

L58 ANSWER 73 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:145560 HCAPLUS

DN 126:233054

TI A nonradioisotope approach to study the in vivo metabolism of **phosphorothioate oligonucleotides**

AU Cohen, Aharon S.; Bourque, Andre J.; Wang, Bing H.; Smisek, David L.; Belenky, Alexei

CS Hybridon, Inc., Worcester, OH, 01605, USA

SO Antisense & Nucleic Acid Drug Development (1997), 7(1), 13-22

CODEN: ANADF5; ISSN: 1087-2906

PB Liebert

DT Journal

LA English

AB A 25-mer **phosphorothioate oligodeoxynucleotide** (GEM 91) complementary to the gag gene mRNA of HIV-1 virus was administered i.v. (IV) at a dose of 10 mg/kg/day for 8 wk or 25 mg/kg single dose s.c. (SC) to adult Rhesus monkeys. No radioactive markers were used. A capillary gel electrophoresis (CGE) method with UV detection was used to determine the concentration of GEM 91 in plasma and the metabolite profile.

The

metabolite profile was virtually the same following a single dose of either 10 mg/kg IV or 25 mg/kg SC. A different metabolite profile was observed after 4 or 8 wk of multiple IV doses of 10 mg/kg/day. The extract was subjected to matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOFMS) for pos. identification. Mass spectrometry confirmed the major metabolic pathway in vivo to be via 3'-end exonuclease activity. The extract was then subjected to a hybridization-assisted ligation reaction in which only 5'-end intact metabolites were labeled. Anal. by CGE with laser-induced fluorescence (LIF) detection allowed each of these metabolites to be quantified with a limit of detection of 1 ppb (ng/mL). MALDI-TOFMS identified components digested from both ends of the DNA. This study demonstrates that the combination of quant. CGE-LIF and MALDI-TOFMS yields a powerful and unique approach to study the metabolism of **phosphorothioate oligonucleotides**.

L58 ANSWER 74 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:751517 HCAPLUS

DN 126:14743

TI Antisense cooperative **oligonucleotides** for improved inhibition of gene expression

IN Kandimalla, Ekambar R.; Agrawal, Sudhir

PA Hybridon, Inc., USA

SO PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

PI WO 9632474 A1 19961017 WO 1996-US4605 19960404 <--
 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
 FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU,
 LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
 SI, SK
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR
 US 6372427 B1 20020416 US 1995-420672 19950412 <--
 AU 9654418 A1 19961030 AU 1996-54418 19960404 <--
 PRAI US 1995-420672 A 19950412 <--
 WO 1996-US4605 W 19960404 <--

AB Disclosed is a composition comprising at least 2 synthetic, cooperative **oligonucleotides**, each comprising a region complementary to one of tandem, non-overlapping regions of a target single-stranded **nucleic acid**, and each further comprising a dimerization domain at a terminus of each of the **oligonucleotides**, the dimerization domains of the **oligonucleotides** being complementary to each other. Also disclosed are duplex structures, ternary complexes, pharmaceutical formulations, and methods utilizing the cooperative **oligonucleotides** of the invention. The antisense **oligonucleotides** are optimized for therapeutic and diagnostic use and have improved sequence specificity for a single-stranded target, reduced toxicity, and improved biol. activity as antisense mols. The cooperative nature of the described **oligonucleotides** was demonstrated from (1) thermal melting studies, (2) their ability to activate RNase H, and (3) their ability to inhibit HIV-1 viral gag mRNA expression or influenza gene expression in cell culture. Modified (**phosphorothioate internucleotide-linked**) **oligonucleotide** combinations with an extended dimerization domain have an enhanced ability to inhibit the expression of the target gene.

L58 ANSWER 75 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:741485 HCAPLUS

DN 126:118135

TI Mixed backbone oligonucleotides containing internucleotidic primary phosphoramidate linkages

AU Devlin, Theresa; Iyer, Radhakrishnan P.; Johnson, Suzanne; Agrawal, Sudhir

CS Hybridon Inc., Worcester, MA, 01605, USA

SO Bioorganic & Medicinal Chemistry Letters (1996), 6(22), 2663-2668
 CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

DT Journal

LA English

AB Mixed backbone oligonucleotides (MBOs) which contain segments of primary phosphoramidate linkages (PO-NH₂) in conjunction with either phosphoric diesters (PO), or phosphorothioates (PS) were prepared Thermal denaturation of the duplexes with RNA and DNA reveal that they form stable duplexes which display cooperative melting profiles. Preliminary stability studies reveal that the PO-NH₂ linkage is resistant to serum nucleases. Thus, these MBOs represent novel antisense mols.

IT 185823-45-4P

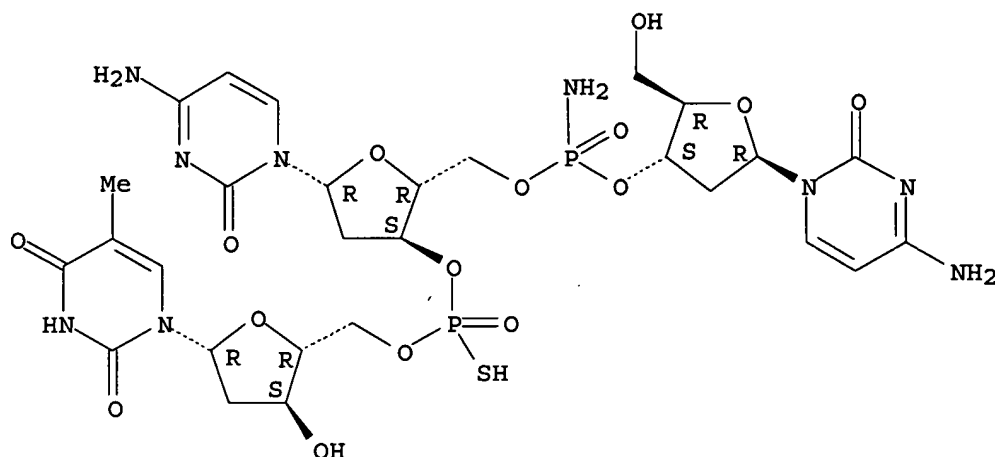
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of mixed backbone oligodeoxyribonucleotides containing internucleotidic primary phosphoramidate linkages)

RN 185823-45-4 HCAPLUS

CN Thymidine, P-amino-P,2'-dideoxycytidylyl-(3'→5')-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 76 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:632215 HCAPLUS
DN 125:267509
TI Human vascular endothelial growth factor gene expression inhibition by
synthetic antisense **oligonucleotides** and retinopathy or
age-related macular degeneration treatment
IN Robinson, Gregory S.
PA **Hybridon, Inc., USA**
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9627006	A2	19960906	WO 1996-US2840	19960229 <--
	WO 9627006	A3	19961017		
	W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE			
	US 5639872	A	19970617	US 1995-398945	19950302 <--
	US 5641756	A	19970624	US 1995-569926	19951208 <--
	AU 9651791	A1	19960918	AU 1996-51791	19960229 <--
	EP 815218	A2	19980107	EP 1996-908608	19960229 <--
	EP 815218	B1	20040421		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE			
	JP 11501508	T2	19990209	JP 1996-526431	19960229 <--
	AT 264912	E	20040515	AT 1996-908608	19960229 <--
PRAI	US 1995-398945	A	19950302	<--	
	US 1995-569926	A	19951208	<--	
	US 1993-98942	A2	19930727	<--	
	US 1995-378860	A2	19950126	<--	
	WO 1996-US2840	W	19960229	<--	

AB Disclosed are **oligonucleotides** complementary to vascular endothelial growth factor (VEGF)-specific **nucleic acid** useful in reducing the expression of VEGF. Also disclosed are pharmaceutical formulations containing such **oligonucleotides** and method useful for treating various disorders associated with neovascularization and

angiogenesis. Retinopathy of prematurity and age-related macular degeneration treatment are given as examples. **Oligonucleotide** derivs. containing **phosphorothioate** or other modified linkages are included.

L58 ANSWER 77 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:494192 HCAPLUS

DN 125:134793

TI Synthesis of stereospecific **oligonucleotide phosphorothioates** and antisense **oligonucleotides**
IN Tang, Jinyan; Roskey, Allysen M.; Agrawal, Sudhir
PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9619572	A1	19960627	WO 1995-US16086	19951212 <--
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2208528	AA	19960627	CA 1995-2208528	19951212 <--
	AU 9645146	A1	19960710	AU 1996-45146	19951212 <--
	EP 807171	A1	19971119	EP 1995-943748	19951212 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	CN 1175281	A	19980304	CN 1995-197690	19951212 <--
PRAI	US 1994-362631		19941222 <--		
	WO 1995-US16086		19951212 <--		

AB Disclosed is a method for synthesizing of stereospecific (Rp) **phosphorothioate oligonucleotides**. In this method, a primer comprising a plurality of **deoxyribonucleotides** and a **ribonucleotide** at the 5' terminal or 5' penultimate position, is annealed to a template. The structure is contacted with a mixture of **deoxynucleoside α - triphosphate** Sp diastereomers and a DNA polymerase to form a PS-Rp **oligodeoxynucleotide** extension which is liberated as a single-stranded PS-Rp **oligonucleotide** by cleavage after the **ribonucleotide** in the primer. Also disclosed are PS-RP **oligonucleotides** and **oligonucleotides** prepared according to this method.

L58 ANSWER 78 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:444144 HCAPLUS

DN 125:108875

TI Preparation of ribozyme analogs containing rigid molecular linkers with increased nuclease resistance

IN Goodchild, John; Leonard, Thomas E.

PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9615240	A2	19960523	WO 1995-US14705	19951108 <--
	WO 9615240	A3	19960815		
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD,				

MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
 TJ, TM
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
 IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
 NE, SN, TD, TG

US 5650502	A	19970722	US 1994-336526	19941109 <--
US 5679555	A	19971021	US 1995-478940	19950607 <--
CA 2204870	AA	19960523	CA 1995-2204870	19951108 <--
AU 9641553	A1	19960606	AU 1996-41553	19951108 <--
EP 791060	A2	19970827	EP 1995-939906	19951108 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
 JP 10509039 T2 19980908 JP 1995-516243 19951108 <--

PRAI US 1994-336526 A 19941109 <--
 WO 1995-US14705 W 19951108 <--

AB Disclosed are ribozyme analogs having the ability to endonucleolytically cleave a sequence of 3' to 5' linked ribonucleotides and increased nuclease resistance. The ribozyme analogs include a plurality of 3' to 5' covalently-linked nucleotides, and a rigid mol. linker having at least one non-nucleotidic mol. covalently linked to two of the nucleotides. Also disclosed are methods of preparing and utilizing the ribozyme analogs of the invention, and pharmaceutical formulations and kits containing such ribozyme analogs. Preparation of a rigid mol. linker trans-1-O-(4,4'-dimethoxytrityl)-2-O-[β -cyanoethoxy-(N,N-diisopropylamino)] phosphino-1,2,-cyclohexanediol and ribozyme analogs was demonstrated.

L58 ANSWER 79 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:380069 HCAPLUS

DN 125:27698

TI Use of 2'-substituted antisense oligonucleotides to down-regulate gene expression

IN Agrawal, Sudhir; Diasio, Robert B.; Zhang, Ruiwen

PA Hybridon, Inc., USA

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9612497	A1	19960502	WO 1995-US13069	19951017 <--
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5591721	A	19970107	US 1994-328520	19941025 <--
	CA 2203652	AA	19960502	CA 1995-2203652	19951017 <--
	AU 9538930	A1	19960515	AU 1995-38930	19951017 <--
	EP 788366	A1	19970813	EP 1995-938213	19951017 <--
	EP 788366	B1	19991215		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1170367	A	19980114	CN 1995-196839	19951017 <--
	JP 10507635	T2	19980728	JP 1995-513977	19951017 <--
	AT 187645	E	20000115	AT 1995-938213	19951017 <--
	ES 2141393	T3	20000316	ES 1995-938213	19951017 <--
	NO 9701905	A	19970624	NO 1997-1905	19970424 <--
	US 6645943	B1	20031111	US 1999-321249	19990527 <--
	GR 3032669	T3	20000630	GR 2000-400367	20000216 <--
	US 2004033980	A1	20040219	US 2003-640898	20030814 <--

- PRAI US 1994-328520 A 19941025 <--
 WO 1995-US13069 W 19951017 <--
 US 1996-709910 B2 19960909 <--
 US 1996-758005 B1 19961127 <--
 US 2000-587934 A3 20000606 <--
- AB A method of down-regulating the expression of a gene in an animal using antisense **oligonucleotides** with non-phosphodiester bonds and a 2'-modified sugar forming the backbone is described. These **oligonucleotide** may be used in therapeutics and in research (as an alternative to preparing knockout animals). A **phosphorothioate oligonucleotide** with 2'-O-methylribose was prepared and administered to rats by gavage. Approx. 80% of the **oligonucleotide** was recovered in feces and urine and no degradation products were obtained from the stomach. Intact **oligonucleotide** was detected in the large intestine and blood plasma.
- L58 ANSWER 80 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:306638 HCAPLUS
 DN 125:26158
 TI **Oligodeoxynucleotides** inhibit retinal neovascularization in a murine model of proliferative retinopathy
 AU Robinson, Gregory S.; Pierce, Eric A.; Rook, Susan L.; Foley, Elliot; Webb, Ruth; Smith, Lois E. H.
 CS **Hybridon, Inc., Worcester, MA, 01605, USA**
 SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(10), 4851-4856
 CODEN: PNASA6; ISSN: 0027-8424
 PB National Academy of Sciences
 DT Journal
 LA English
 AB Diseases characterized by retinal neovascularization are among the principal causes of visual loss worldwide. The hypoxia-stimulated expression of vascular endothelial growth factor (VEGF) has been implicated in the proliferation of new blood vessels. We have investigated the use of antisense **phosphorothioate oligodeoxynucleotides** against murine VEGF to inhibit retinal neovascularization and VEGF synthesis in a murine model of proliferative retinopathy. Intravitreal injections of two different antisense **phosphorothioate oligodeoxynucleotides** prior to the onset of proliferative retinopathy reduced new blood vessel growth a mean of 25 and 31% compared with controls. This inhibition was dependent on the concentration of antisense **phosphorothioate oligodeoxynucleotides** and resulted in a 40-66% reduction of the level of VEGF protein, as determined by Western blot anal. Control (sense, nonspecific) **phosphorothioate oligodeoxynucleotides** did not cause a significant reduction in retinal neovascularization or VEGF protein levels. These data further establish a fundamental role for VEGF expression in ischemia-induced proliferative retinopathies and a potential therapeutic use for antisense **phosphorothioate oligodeoxynucleotides**.
- L58 ANSWER 81 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:285360 HCAPLUS
 DN 125:1094
 TI Antisense-mediated inhibition of protein synthesis. Rational drug design, pharmacokinetics, intracerebral application, and organ uptake of **phosphorothioate oligodeoxynucleotides**
 AU Brysch, Wolfgang; Rifai, Abdalla; Tischmeyer, Wolfgang; Schlingensiepen, Karl-Hermann
 CS Max-Planck Institute Biophysical Chemistry, Goettingen, Germany
 SO Antisense Therapeutics (1996), 159-182. Editor(s): **Agrawal, Sudhir**. Publisher: Humana, Totowa, N. J.
 CODEN: 62TUA7

DT Conference
 LA English
 AB This chapter focuses on the quantification, time-course, and specificity of antisense-mediated inhibition of protein synthesis. Cellular uptake of the **phosphorothioate oligonucleotides** was also studied in culture and in vivo following i.v. or intracerebral injection. The efficient neuronal uptake and intraneuronal protein suppression observed for the **oligonucleotides** studied are encouraging with respect to the development of antisense pharmaceuticals for the treatment of neurol. disorders and other diseases localized to the CNS, including tumors.

L58 ANSWER 82 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:256086 HCAPLUS

DN 124:317787

TI Purification of **oligodeoxynucleotide phosphorothioates** using DEAE 5PW anion ion-exchange chromatography and hydrophobic interaction chromatography

IN Puma, Patricia; Duffey, Dan; Dawidczyk, Paul

PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9601268	A1	19960118	WO 1995-US8175	19950630 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2194350	AA	19960118	CA 1995-2194350	19950630 <--
	AU 9529523	A1	19960125	AU 1995-29523	19950630 <--
	EP 765334	A1	19970402	EP 1995-925363	19950630 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1155887	A	19970730	CN 1995-194675	19950630 <--
	JP 10505577	T2	19980602	JP 1995-503914	19950630 <--
PRAI	US 1994-270582		19940705 <--		
	WO 1995-US8175		19950630 <--		

AB **Oligonucleotide phosphorothioates** are purified by a method comprising applying a mixture of the **oligonucleotide** to a column containing a DEAE-5PW anion ion-exchange chromatog. resin and eluting with an elution buffer having a concentration of sodium chloride of from about 0-2M. In other aspects of the invention, **oligonucleotide phosphorothioates** are purified by a method comprising applying a mixture of the **oligonucleotide** to a column containing a phenyl-Sepharose fast flow chromatog. resin or a phenyl-5PW chromatog. resin and eluting with an elution buffer substantially free of salts. This improved method for separating and purifying **oligonucleotide phosphorothioates** provides the ability to purify ammoniacal solns. of **oligonucleotides** inexpensively, quickly, and on a large scale. Thus, a 25-mer **oligonucleotide phosphorothioate** having the sequence CTCTCGACCCATCTCTCCTTCT was purified using a 0.51 L column of 30 µm TSK DEA 5PW (TosoHaas). The resin was packed into a Pharmacia 5.0 cm diameter glass column. In one experiment, elution was performed with 25 mM Tris-HCl (pH 7.2) containing 2 M NaCl to give the **oligonucleotide** of 99.2% purity in 96.2% recovery.

L58 ANSWER 83 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:190896 HCAPLUS
 DN 124:220481
 TI Antisense **oligonucleotides** and methods for the treatment of schistosomiasis
 IN **Agrawal, Sudhir**; Tang, Jin-Yan; Tao, Liang-Feng; Marx, Kenneth A.; Coleman, Robert
 PA **Hybridon, Inc., USA**; University of Massachusetts at Lowell
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9533759	A2	19951214	WO 1995-US9598	19950530 <--
	WO 9533759	A3	19960111		
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT			
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9532052	A1	19960104	AU 1995-32052	19950530 <--
PRAI	US 1994-252275		19940601 <--		
	WO 1995-US9598		19950530 <--		
AB	Antisense oligonucleotides effective at inhibiting protein synthesis of schistosome worms are disclosed. It is shown that these oligonucleotides are efficiently taken up by the schistosome worm and may effectively kill the worms in vivo. Accordingly, these antisense oligonucleotides and methods of their administration may be useful for treating schistosomiasis.				

L58 ANSWER 84 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:135699 HCAPLUS
 DN 124:194345
 TI Use of **oligonucleotide phosphorothioates** for depleting complement and for reducing blood pressure
 IN Galbraith, Wayne M.; **Agrawal, Sudhir**
 PA **Hybridon, Inc., USA**
 SO PCT Int. Appl., 53 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9532719	A1	19951207	WO 1995-US6161	19950519 <--
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UZ			
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	CA 2191192	AA	19951207	CA 1995-2191192	19950519 <--
	AU 9525914	A1	19951221	AU 1995-25914	19950519 <--
	EP 760666	A1	19970312	EP 1995-920471	19950519 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
	CN 1153476	A	19970702	CN 1995-194229	19950519 <--
	JP 10501224	T2	19980203	JP 1995-500924	19950519 <--
PRAI	US 1994-250853		19940527 <--		
	WO 1995-US6161		19950519 <--		

AB Methods are disclosed for reducing blood pressure, stimulating vasodilation, and depleting complement in primates. These methods involve administering an **oligonucleotide** to the primate, and then measuring the decrease in blood pressure or complement activity. The **oligonucleotide** being administered is 2-50 **nucleotides** in length and has at least one **phosphorothioate internucleotide linkage**.

L58 ANSWER 85 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:996966 HCAPLUS

DN 124:146756

TI Purification of **oligodeoxynucleotide phosphorothioates** using anion exchange chromatography

IN Tang, Jin-Yan; Guo, Que; Agrawal, Sudhir

PA Hybridon, Inc., USA

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9527718	A2	19951019	WO 1995-US4492	19950407 <--
	WO 9527718	A3	19951102		
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT			
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	CA 2187338	AA	19951019	CA 1995-2187338	19950407 <--
	AU 9522867	A1	19951030	AU 1995-22867	19950407 <--
	EP 755400	A1	19970129	EP 1995-916332	19950407 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
	CN 1150431	A	19970521	CN 1995-193486	19950407 <--
	JP 10502052	T2	19980224	JP 1995-526519	19950407 <--
PRAI	US 1994-225475		19940408 <--		
	WO 1995-US4492		19950407 <--		

AB The present invention provides improved methods for separating and purifying **oligonucleotide phosphorothioates**, which is suitable for large scale separation. For the first time, authors used a DMAE Fractogel EMD ion-exchange chromatog. column which eliminate the necessity of using an elution buffer containing organic solvents. By varying the conditions employed,

excellent separation can be obtained. In particular, authors have been able to use a higher pH and lower salt concns. than previously reported in the literature to obtain chromatog. separation of **oligonucleotide phosphorothioates** having length up to about 35 **nucleotides**.

This method is also advantageous because it does not require elevated temps., making it more amenable for large scale chromatog. Thus, a mixture of **oligonucleotide phosphorothioates** having sequences of CTCTCGCACCCATCT (I), CTCTCGCACCCATCTCTCTC (II), and CTCTCGCACCCATCTCTCTCTCT (III) was loaded on a 1.5 cm ID DMAE Fractogel EMD ion-exchange column (particle size 25-40 µm, E. Merck separation) and eluted with a linear flow of 5 mL/min using a buffer A [25 mM Tris-HCl (pH 8.0) containing 205 50 mM aqueous solution of mannitol] and buffer B (buffer A

and 2

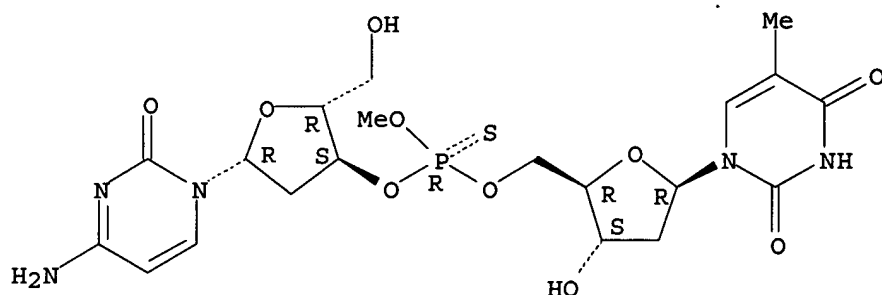
M NaCl). The retention times were 29.66, 42.4, and 52.67 min for 15mer I, 20mer II, and 25mer III, resp.

L58 ANSWER 86 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:950191 HCAPLUS

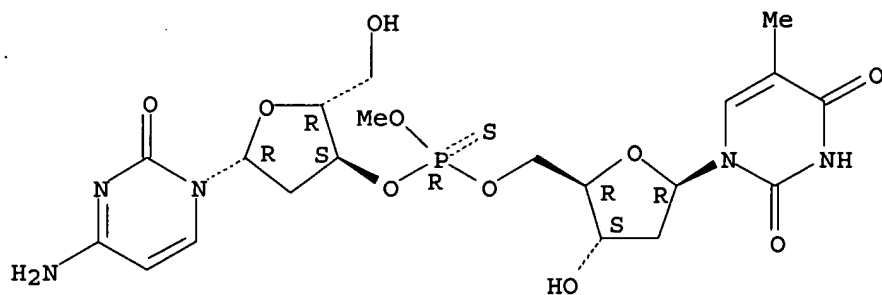
DN 124:146710
 TI O- and S-Methyl Phosphotriester Oligonucleotides: Facile Synthesis Using
 N-Pent-4-enoyl Nucleoside Phosphoramidites
 AU Iyer, Radhakrishnan P.; Yu, Dong; Ho, Nan-Hui; Devlin, Theresa;
 Agrawal, Sudhir
 CS Hybridon Inc., Worcester, MA, 01605, USA
 SO Journal of Organic Chemistry (1995), 60(25), 8132-3
 CODEN: JOCEAH; ISSN: 0022-3263
 PB American Chemical Society
 DT Journal
 LA English
 AB Reported herein is a practical methodol. for the synthesis of,
 support-bound and free, O- as well as S-methylphosphotriester
 oligonucleotides using N-pent-4-enoyl nucleoside phosphoramidites.
 IT 173346-60-6DP, polymer support 173346-60-6P
 173401-22-4DP, polymer support 173401-22-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of oligodeoxyribonucleotide phosphotriesters using pentenoyl as
 protective group)
 RN 173346-60-6 HCAPLUS
 CN Thymidine, 2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')-, (R)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



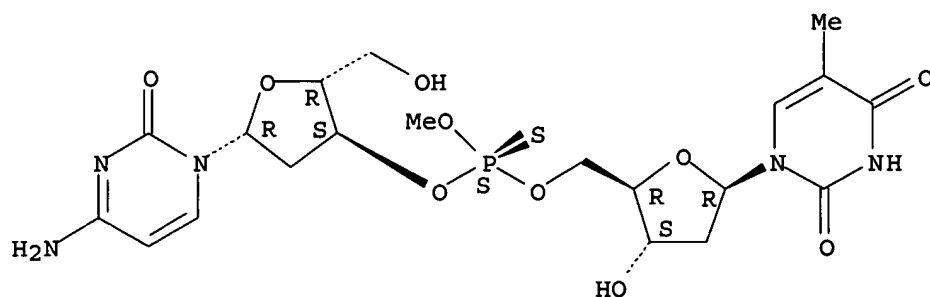
RN 173346-60-6 HCAPLUS
 CN Thymidine, 2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')-, (R)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 173401-22-4 HCAPLUS
 CN Thymidine, 2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')-, (S)-
 (9CI) (CA INDEX NAME)

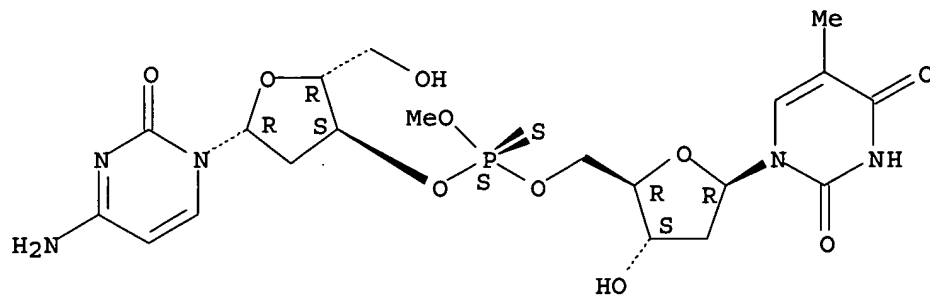
Absolute stereochemistry.



RN 173401-22-4 HCAPLUS

CN Thymidine, 2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')-, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L58 ANSWER 87 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:863721 HCAPLUS

DN 123:275995

TI Antisense **oligonucleotides** to the BZLF1 gene that inhibit
Epstein-Barr virus replication

IN Mulder, Carel

PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9522554	A1	19950824	WO 1995-US2082	19950217 <--
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CN, CZ, DE, DK, EE, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN			
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5550047	A	19960827	US 1994-199510	19940218 <--
	AU 9518789	A1	19950904	AU 1995-18789	19950217 <--
PRAI	US 1994-199510		19940218 <--		
	WO 1995-US2082		19950217 <--		

AB **Oligonucleotides** complementary to a portion of the BZLF1 RNA of Epstein-Barr virus, useful for inhibiting the induction of the lytic cycle in EBV-infected cells, and in inhibiting EBV replication are described. In vitro expts. using **phosphodiester**- and

phosphorothioate-linked oligonucleotides are reported. Dose-dependent inhibition of viral replication was observed with the **phosphorothioate oligonucleotides** being the more effective.

L58 ANSWER 88 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:858806 HCAPLUS

DN 123:246807

TI **Oligonucleotides** with anti-respiratory syncytial virus activity

IN Kilkuskie, Robert E.; Brown-Vargas, Patrick E.

PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9522553	A1	19950824	WO 1995-US2080	19950217 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CN, CZ, DE, DK, EE, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2181546	AA	19950824	CA 1995-2181546	19950217 <--
	AU 9518788	A1	19950904	AU 1995-18788	19950217 <--
	EP 745090	A1	19961204	EP 1995-911046	19950217 <--
	EP 745090	B1	19970827		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 157370	E	19970915	AT 1995-911046	19950217 <--
	JP 09509181	T2	19970916	JP 1995-521953	19950217 <--
PRAI	US 1994-199503		19940218 <--		
	WO 1995-US2080		19950217 <--		

AB **Oligonucleotides** that hybridize to a portion of respiratory syncytial virus (RSV) genomic RNA under physiolo. conditions, and, in doing so, inhibit viral replication are described for use in the inhibition of viral replication. Also disclosed are pharmaceutical compns. and methods useful for inhibiting and treating RSV infection and including at least one or two of these **oligonucleotides**, or at least one of these **oligonucleotides** and ribavirin.

L58 ANSWER 89 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:845945 HCAPLUS

DN 123:265957

TI Use of cyclodextrin and its derivatives as carriers for **oligonucleotide** delivery

AU **Zhao, Qiuyan; Temsamani, Jamal; Agrawal, Sudhir**

CS **Hybridon, Inc., Worcester, MA, 01605, USA**

SO Antisense Research and Development (1995), 5(3), 185-92

CODEN: AREDEI; ISSN: 1050-5261

PB Liebert

DT Journal

LA English

AB The use of antisense **phosphorothioate oligodeoxynucleotides** as tools for modulating gene expression represents a novel strategy for designing drugs to treat a variety of diseases. Several factors, including cellular uptake and internalization of the **phosphorothioate oligodeoxynucleotide**, are important parameters in determining the effectiveness of antisense agents as therapies. We have used cyclodextrin and its analogs as carriers to increase cellular uptake of **phosphorothioate oligodeoxynucleotides**. The studies were carried out using

35S-labeled and fluorescent-labeled **phosphorothioate oligodeoxynucleotide** in human T cell leukemia H9 cell line.

Cellular uptake of **phosphorothioate oligodeoxynucleotide** in the presence of cyclodextrin was found to be concentration and time dependent.

Using various cyclodextrin analogs, e.g., 2-hydroxypropyl β -cyclodextrin (HPCD), hydroxyethyl β -cyclodextrin (HECD), and a mixture of various hydroxypropyl β -cyclodextrins (Encapsin), we observed increases in **phosphorothioate oligodeoxynucleotide** uptake, up to two- to three-fold in 48 h. Confocal microscopy studies confirmed that **oligonucleotide** was present intracellularly. Cyclodextrin itself was not toxic at the concentration used. Cyclodextrins did not seem to affect the efflux of **phosphorothioate oligodeoxynucleotide** from cells. Stability of **phosphorothioate oligodeoxynucleotide** against endogenous cellular nucleases remained unchanged in the presence of cyclodextrins. These studies suggest that cyclodextrin and its analogs might be used successfully as carriers for **oligonucleotide** and analogs.

L58 ANSWER 90 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:836335 HCAPLUS

DN 124:134823

TI Design, biochemical, biophysical and biological properties of cooperative antisense **oligonucleotides**

AU Kandimalla, Ekambar R.; Manning, Adrienne; Lathan, Christopher; Byrn, Randal A.; Agrawal, Sudhir

CS Hybridon, Inc., Worcester, MA, 01604, USA

SO Nucleic Acids Research (1995), 23(17), 3578-84

CODEN: NARHAD; ISSN: 0305-1048

PB Oxford University Press

DT Journal

LA English

AB Short **oligonucleotides** that can bind to adjacent sites on target mRNA sequences are designed and evaluated for their binding affinity and biol. activity. Sequence-specific binding of short tandem **oligonucleotides** is compared with a full-length single **oligonucleotide** (21mer) that binds to the same target sequences. Two short **oligonucleotides** that bind without a base separation between their binding sites on the target bind cooperatively, while **oligonucleotides** that have a one or two base separation between the binding **oligonucleotides** do not. The binding affinity of the tandem **oligonucleotides** is improved by extending the ends of the two **oligonucleotides** with complementary sequences. These extended sequences form a duplex stem when both **oligonucleotides** bind to the target, resulting in a stable ternary complex. RNase H studies reveal that the cooperative **oligonucleotides** bind to the target, resulting in a stable ternary complex. RNase H studies reveal that the cooperative **oligonucleotides** bind to the target RNA with sequence specificity. A short **oligonucleotide** (9mer) with one or two mismatches does not bind at the intended site, while longer **oligonucleotides** (21mers) with one or two mismatches still bind to the same site, as does a perfectly matched 21mer, and evoke RNase H activity. HIV-1 inhibition studies reveal an increase in activity of the cooperative **oligonucleotide** combinations as the length of the dimerization domain increases.

L58 ANSWER 91 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:828510 HCAPLUS

DN 123:222306

TI Separation of **oligonucleotide** analogs by high-performance capillary electrophoresis with high concentrations of urea and organic solvent

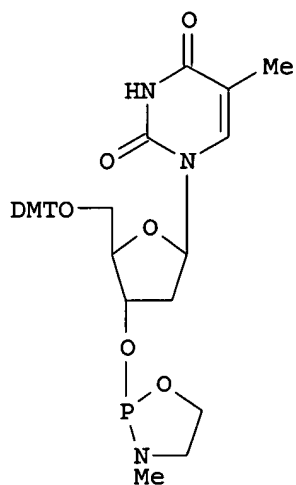
IN Cohen, Aharon S.; Bourque, Andre; Vilenchik, Maria

PA **Hybridon, Inc., USA**
 SO PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9518813	A1	19950713	WO 1995-US163	19950104 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CN, CZ, DE, DK, EE, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5627277	A	19970506	US 1994-178660	19940107 <--
	AU 9514493	A1	19950801	AU 1995-14493	19950104 <--
	EP 738272	A1	19961023	EP 1995-906176	19950104 <--
	EP 738272	B1	19971105		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09507574	T2	19970729	JP 1995-518609	19950104 <--
PRAI	US 1994-178660		19940107 <--		
	US 1992-991466		19921216 <--		
	US 1993-32856		19930316 <--		
	WO 1995-US163		19950104 <--		
AB	<p>A substrate is provided useful for separating unmodified and modified mononucleotides and oligonucleotides. The substrate includes $\geq 12\%$ (weight: volume) polymer (e.g., polyacrylamide, methylcellulose, or polyvinyl alc.) in $\geq 5M$ urea and $\geq 32\%$ (volume: volume) organic solvent, the organic solvent being a chemical stable liquid at room temperature and having a dielec. constant of ≥ 20. Also provided is a high-performance capillary electrophoretic method of separating unmodified and modified mononucleotides and/or oligonucleotides utilizing this substrate and an elec field of >200 V/cm. The method enables separation of oligonucleotides analogs differing in length by only one base or differing in their state of oxidation by only one oxidized nonbridging group. Phosphorothioate oligonucleotide 20-25-mer analogs, polyadenylic acid acid homopolymers of 19-24 bases in length, and their mixts. are resolved on (1) 10 cm 12.6% T acrylamide capillaries containing 40.5% DMSO and 7.4M urea at 800 V/cm and 3 μA, (2) on 10 cm 14% T acrylamide capillaries containing 14-56% DMSO and 5.0M urea at 800 V/cm, or (3) on 10 cm 11.4 T acrylamide capillaries containing 74% formamide and 4.7M urea at 400 V/cm and 4 μA.</p>				
L58	ANSWER 92 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN				
AN	1995:770380 HCAPLUS				
DN	123:187771				
TI	Antisense phosphorothioate oligodeoxynucleotides alter HIV type 1 replication in cultured human macrophages and peripheral blood mononuclear cells				
AU	Weichold, Frank F.; Lisziewicz, Julianna; Zeman, Robert A.; Nerurkar, Lata S.; Agrawal, Sudhir; Reitz, Marvin S. Jr.; Gallo, Robert C.				
CS	Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, MD, 20892, USA				
SO	AIDS Research and Human Retroviruses (1995), 11(7), 863-7 CODEN: ARHRE7; ISSN: 0889-2229				
PB	Liebert				
DT	Journal				
LA	English				
AB	The use of antisense oligodeoxynucleotides as antiviral drugs to combat HIV-1 infection may offer an alternative to traditional pharmacol. therapies. The authors compared the effects of two 28-mer antisense				

phosphorothioate oligodeoxynucleotides [PS-oligo(dN)] with non-sequence-specific controls on HIV-1 replication in long-term human monocyte/macrophage and peripheral blood mononuclear cells (PBMC) cultures. The anti-rev PS-oligo(dN) was complementary to the mRNA sequences derived from the overlapping region of the HIV-1 regulatory genes tat and rev, while anti-gag targeted the translational initiation site of the gag mRNA. In vitro cytotoxicity of the PS-oligo(dN) was evaluated at concns. ranging from 0.1 to 10.0 μ M for a period of 20 days. Cell survival was 100% at 0.1 μ M, but decreased to 5% at 10.0 μ M in relation to the untreated control cultures. The data demonstrate that replication of both the T cell-tropic and macrophage-tropic HIV-1 strains in primary cells can be inhibited by PS-oligo(dN) in a sequence-specific and dose-dependent manner at concns. achievable in vivo. However, the sequence-dependent antiviral activity of the utilized PS-oligo(dN) was limited to a window of specificity at concns. between 0.25 and 1.0 μ M.

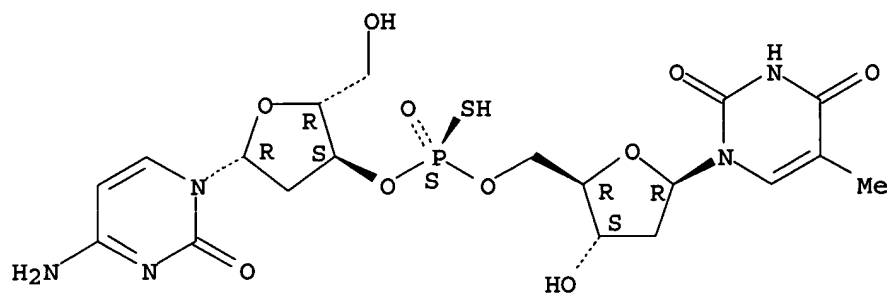
L58 ANSWER 93 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:746933 HCAPLUS
 DN 124:9272
 TI Nucleoside Oxazaphospholidines as Novel Synthons in Oligonucleotide Synthesis
 AU Iyer, Radhakrishnan P.; Yu, Dong; Devlin, Theresa; Ho, Nan-Hui; Agrawal, Sudhir
 CS Hybridon Inc., Worcester, MA, 01605, USA
 SO Journal of Organic Chemistry (1995), 60(17), 5388-9
 CODEN: JOCEAH; ISSN: 0022-3263
 PB American Chemical Society
 DT Journal
 LA English
 GI



I

AB Synthons oxazaphospholidines, e.g. I, are a new class of nucleoside monomers for the synthesis of oligodeoxyribonucleotides.
 IT 116113-27-0P 116182-01-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of nucleoside oxazaphospholidines as novel synthons for oligodeoxyribonucleotide)
 RN 116113-27-0 HCAPLUS
 CN Thymidine, [P(S)]-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

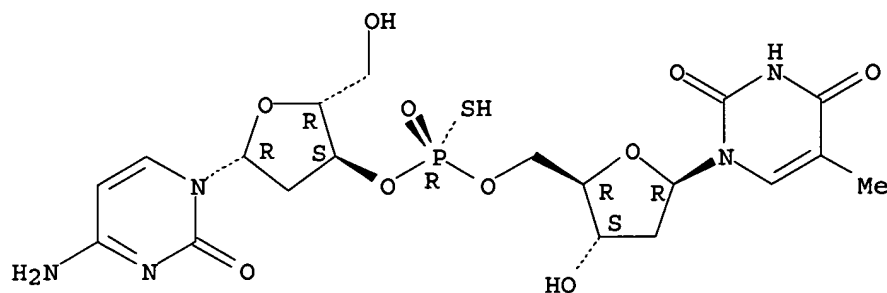
Absolute stereochemistry.



RN 116182-01-5 HCAPLUS

CN Thymidine, [P(R)]-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



L58 ANSWER 94 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:632256 HCAPLUS

DN 123:25684

TI Using antisense **oligonucleotides** to modulate nerve growth and to reverse A4 amyloid-induced morphology

IN Marotta, Charles A.; Majocha, Ronald E.; **Agrawal, Sudhir**

PA General Hospital Corp., USA; **Hybridon, Inc.**

SO PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9509236	A1	19950406	WO 1994-US10943	19940928	<--
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW:	KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2171553	AA	19950406	CA 1994-2171553	19940928	<--
	AU 9478451	A1	19950418	AU 1994-78451	19940928	<--
	EP 721503	A1	19960717	EP 1994-929366	19940928	<--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1136327	A	19961120	CN 1994-194295	19940928	<--
	JP 09505465	T2	19970603	JP 1994-510425	19940928	<--
	US 5670634	A	19970923	US 1995-456420	19950601	<--
	NO 9601262	A	19960328	NO 1996-1262	19960328	<--

PRAI US 1993-128035 19930928 <--
 WO 1994-US10943 19940928 <--

AB **Oligonucleotides** that inhibit the expression of the genes for β /A4 peptide of Alzheimer's disease and Down's Syndrome, and nerve growth factor (NGF) and that reverse morphol. changes caused by β /A4 peptide accumulation in neural cells are described. These **oligonucleotides** may have **phosphorothioate** or other unusual linkages and modified termini or self-complementary ends to stabilize them against nucleases. Pharmaceutical compns., kits and methods for treatment of β /A4 amyloid-induced morphol. as well as an assay for screening candidate antisense **oligonucleotides** effective in the treatment of the deleterious effects that are visited upon cells by β /A4 amyloid peptide are described. The ability of a number of **phosphorothioate oligonucleotides** to inhibit expression of the amyloid A4 gene in PC12 cells carrying an overexpression construct in a dose-dependent manner is demonstrated. Effective levels of the **oligonucleotide** also led to recovery of normal cell morphol.

L58 ANSWER 95 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:540626 HCAPLUS

DN 122:307617

TI Potent antiviral activity of an antisense **oligonucleotide** complementary to the intron-exon boundary of human cytomegalovirus genes UL36 and UL37

AU Pari, Gregory S.; Field, A. Kirk; Smith, Jean A.

CS **Hybridon Inc., Worcester, MA, 01605, USA**

SO Antimicrobial Agents and Chemotherapy (1995), 39(5), 1157-61

CODEN: AMACCQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

AB An antisense **phosphorothioate oligonucleotide** complementary to the intron-exon boundary of human cytomegalovirus genes UL36 and UL37 (UL36ANTI) reduced the yield of infectious virus by 99% and inhibited human cytomegalovirus DNA replication at a concentration of 0.08 μ M. In addition, **oligonucleotides** with base substitutions which resulted in base pair mismatches showed lesser degrees of activity, indicating a sequence-sp. antisense mechanism. UL36ANTI was also shown to inhibit DNA replication of ganciclovir-resistant strains and human cytomegalovirus clin. isolates.

L58 ANSWER 96 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:502931 HCAPLUS

DN 123:9871

TI Synthesis of dimer blocks and their use in assembling oligonucleotides

IN Tang, Jin-yan; Iadarola, Patricia L.; Agrawal, Sudhir

PA **Hybridon, Inc., USA**

SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9415946	A1	19940721	WO 1994-US296	19940107
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2153505	AA	19940721	CA 1994-2153505	19940107
	AU 9460243	A1	19940815	AU 1994-60243	19940107
	AU 673051	B2	19961024		

EP 678096	A1	19951025	EP 1994-906568	19940107
EP 678096	B1	19970319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1122137	A	19960508	CN 1994-191181	19940107
JP 08507752	T2	19960820	JP 1994-516255	19940107
AT 150464	E	19970415	AT 1994-906568	19940107
ES 2100051	T3	19970601	ES 1994-906568	19940107
FI 9503363	A	19950707	FI 1995-3363	19950707
PRAI US 1993-2823	A2	19930108		
WO 1994-US296	W	19940107		

OS MARPAT 123:9871

AB Dimer blocks having an alkylphosphonate, phosphoramidate, phosphorothioate or alkylphosphonothioate internucleotide linkage are prepared by condensing a 1st nucleoside derivative having a protective group at a 5' end and a condensing group at a 3' end with a second nucleoside derivative having a protective group at a 3' end and a hydroxyl group at a 5' end to form a dinucleotide derivative having a reduced internucleotide linkage, and oxidizing the internucleotide linkage with an appropriate oxidizing agent. 5'-O-dimethoxytritylthymidine-3'-O-Me N,N-diisopropylphosphoramidite and N4-benzoyl-3'-O-(tert-butyldimethylsilyl)-2'-deoxycytidine to give in 2 steps the title dimer 5'-O-(dimethoxytrityl)thymidine-3'-O-Me phosphorothioate-5'-O-N4-benzoyl-2'-deoxycytidine (I). PCl3 was added to triazole in CH2Cl2 followed by 4-methylmorpholine and to the mixture was added I to give the H-phosphonate of I (II). I and II were used in the synthesis of the oligonucleotide 5'-CtctcGCACCCAtctctctcCTtcT-3'; at the lower case letters coupling was carried out using I, the rest of the sequence was assembled using H-phosphonates. After the assembly of the above sequence, CPG bound oligomer was oxidized using 5% S in Et3N/pyridine/CS2 to convert H-phosphonate linkages to phosphorothioate linkages, MEO were removed by treatment with PhSH and deprotection with concentrated NH4OH at 55° for 10 h.

IT 162432-01-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of dimer blocks and their use in assembling oligonucleotides)

RN 162432-01-1 HCAPLUS

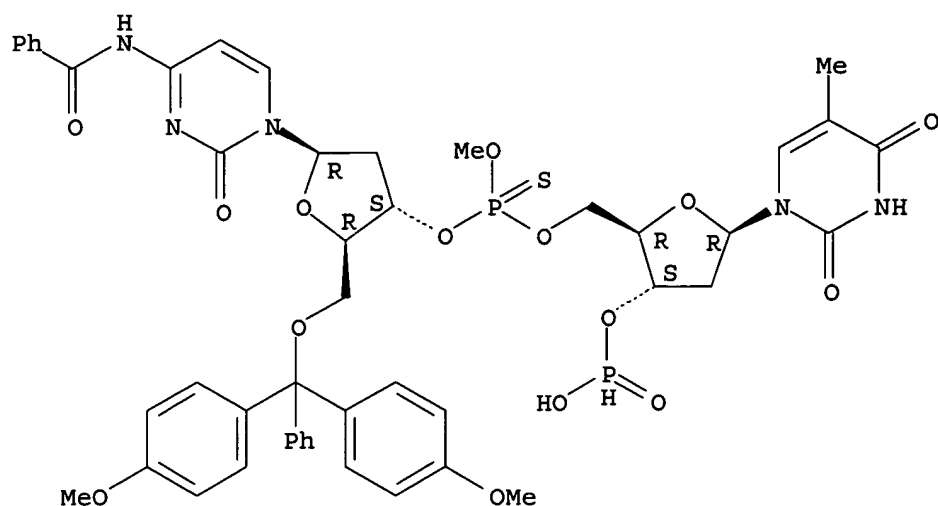
CN Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-P(O)-methyl-P-thiocytidylyl-(3'→5')-, 3'-(hydrogen phosphonate), compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 162432-00-0

CMF C48 H51 N5 O15 P2 S

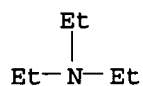
Absolute stereochemistry.



CM 2

CRN 121-44-8

CMF C6 H15 N



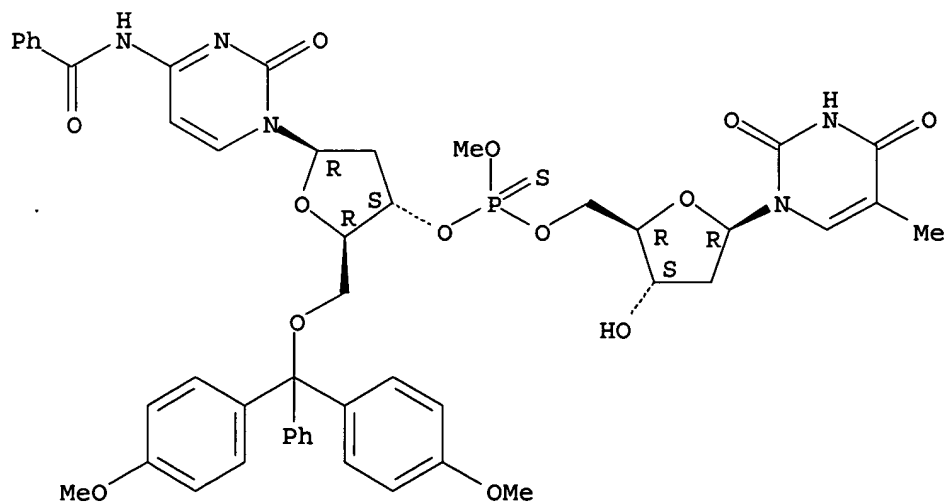
IT 162431-92-7P 162431-93-8P 162431-97-2P
162491-21-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of dimer blocks and their use in assembling
oligonucleotides)

RN 162431-92-7 HCAPLUS

CN Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-P(O)-
methyl-P-thiocytidylyl-(3'→5')-(9CI) (CA INDEX NAME)

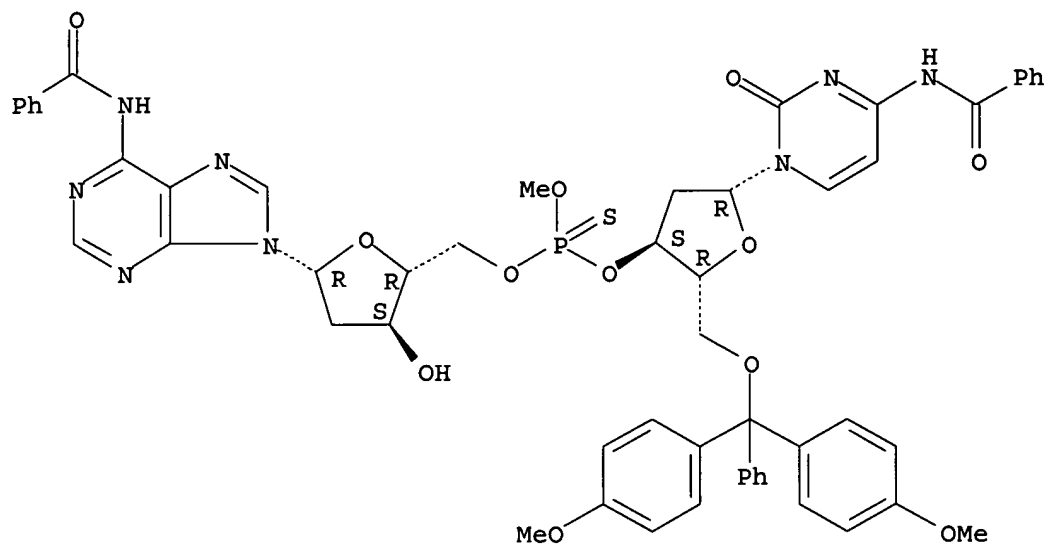
Absolute stereochemistry.



RN 162431-93-8 HCAPLUS

CN Adenosine, N-benzoyl-5'-O- [bis (4-methoxyphenyl) phenylmethyl] -2'-deoxy-P(O) -methyl-P-thiocytidylyl- (3'→5') -N-benzoyl-2'-deoxy- (9CI) (CA INDEX NAME)

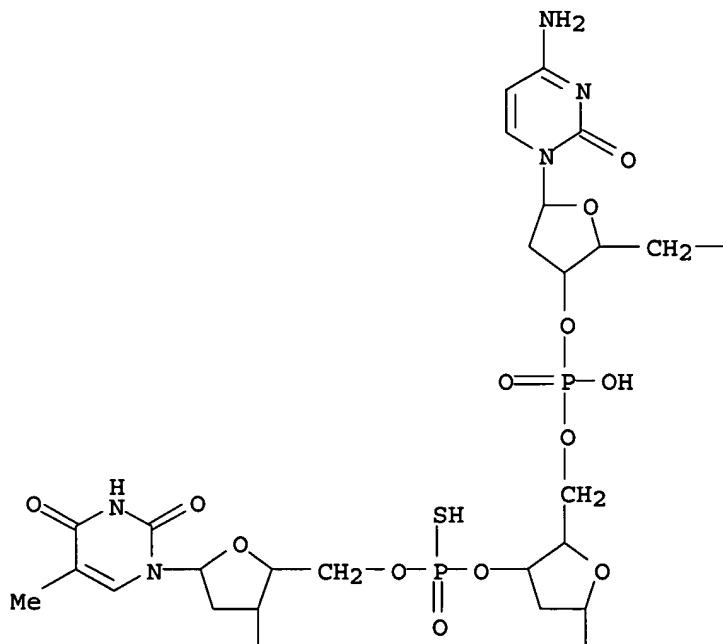
Absolute stereochemistry.



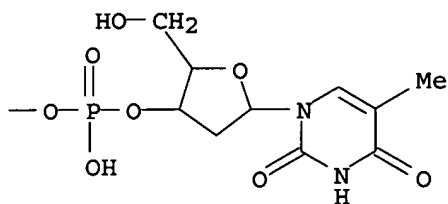
RN 162431-97-2 HCAPLUS

CN Thymidine, thymidylyl- (3'→5') -2'-deoxycytidylyl- (3'→5') -2'-deoxy-P-thiocytidylyl- (3'→5') -thymidylyl- (3'→5') -thymidylyl- (3'→5') -2'-deoxycytidylyl- (3'→5') - (9CI) (CA INDEX NAME)

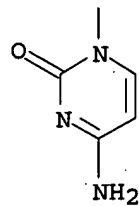
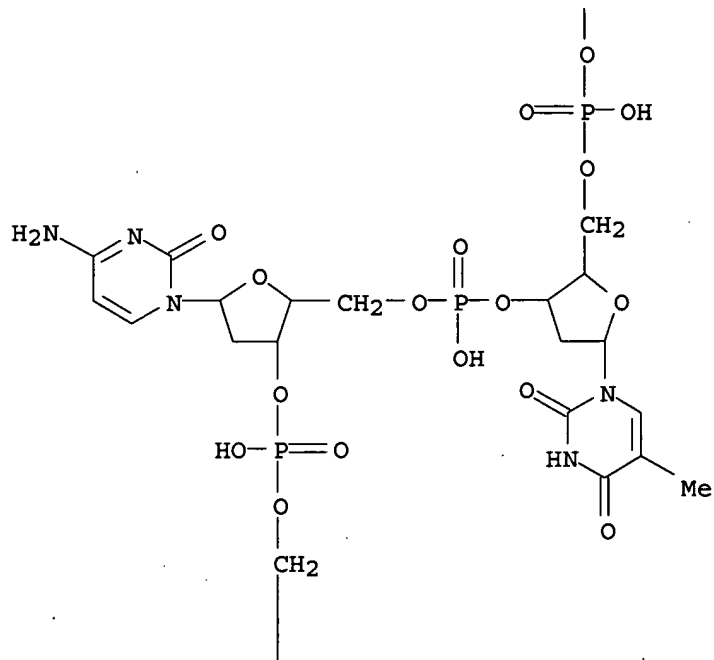
PAGE 1-A



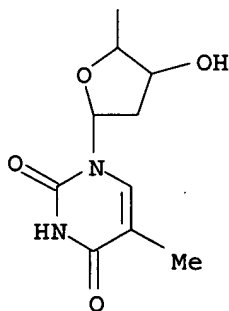
PAGE 1-B



PAGE 2-A

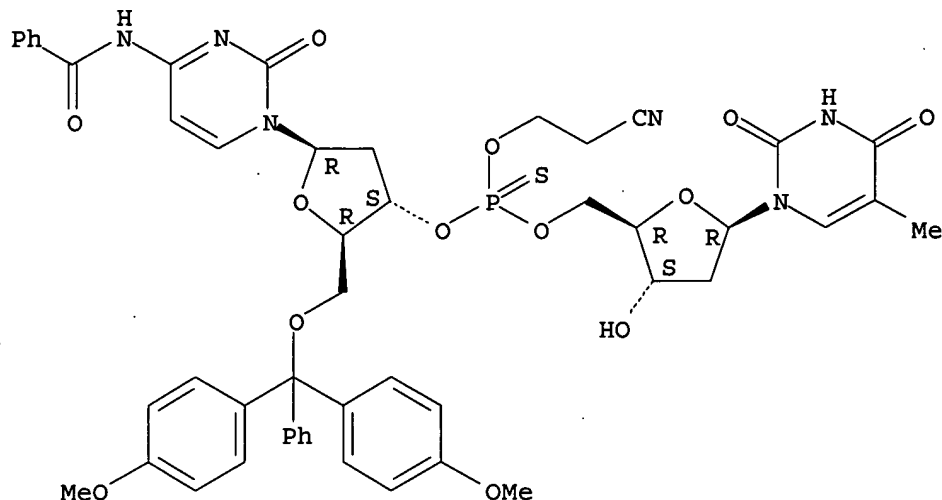


PAGE 3-A



CN Thymidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P(O)-(2-cyanoethyl)-2'-deoxy-P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L58 ANSWER 97 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:401868 HCAPLUS

DN 122:204281

TI Pharmacokinetics of antisense **oligonucleotides**

AU **Agrawal, Sudhir**; Temsamani, Jamal; Galbraith, Wayne; Tang, Jinyan

CS **Hybridon Inc., Worcester, MA, USA**

SO Clinical Pharmacokinetics (1995), 28(1), 7-16

CODEN: CPKNDH; ISSN: 0312-5963

DT Journal; General Review

LA English

AB A review with 27 refs. Antisense **oligonucleotides** are promising therapeutic agents for the treatment of life-threatening diseases. I.v. injection of **phosphodiester oligonucleotide** analog (P-**oligonucleotide**) in monkeys shows that the **oligonucleotide** is degraded rapidly in the plasma with a half-life of about 5 min. Administration of a single dose of the **phosphorothioate oligonucleotide** in animals by the i.v. route reveals biphasic plasma elimination. An initial short half-life (0.53 to 0.83 h) represents distribution out of the plasma compartment and a second long half-life (35 to 50 h) represents elimination from the body. This elimination half-life was similar when the **oligonucleotide** was administered s.c. In contrast, **methylphosphonate oligonucleotides** have an elimination half-life of 17 min in mice. **Phosphorothioate oligonucleotides** were distributed into most of organs of rats and mice. Liver and kidney were the 2 organs with highest uptake of the **oligonucleotide**. The **phosphorothioate oligonucleotides** were primarily excreted in urine. Greater than 30% was excreted in the first 24 h. Repeated daily i.v. injections of a 25-mer **phosphorothioate oligonucleotide** into rats showed that the concns. in the plasma are at steady-state during the 8 days' administration. The data represented here support the potential utility of **phosphorothioate** and **methylphosphonate oligonucleotides** as therapeutic agents in vivo.

- L58 ANSWER 98 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:139338 HCAPLUS
DN 122:95897
TI Complement activation and hemodynamic changes following intravenous administration of **phosphorothioate oligonucleotides** in the monkey
AU Galbraith, Wayne M.; Hobson, William C.; Giclas, Patricia C.; Schechter, Paul J.; **Agrawal, Sudhir**
CS APD Co., Arlington, VA, 22209, USA
SO Antisense Research and Development (1994), 4(3), 201-6
CODEN: AREDEI; ISSN: 1050-5261
DT Journal
LA English
AB Rapid i.v. infusion of GEM 91, a 25-mer **phosphorothioate oligonucleotide** complementary to the gag site of HIV, in the monkey produces transient decreases in peripheral total WBC and neutrophil counts, hemoconcn., and a brief increase followed by a prolonged decrease in arterial blood pressure. These changes are preceded by and are likely mediated by activation of C5 complement. These effects are dose and infusion rate dependent and can be avoided by administering GEM 91 by slow i.v. infusion. Similar hemodynamic effects are produced with rapid i.v. infusion of other **phosphorothioate oligonucleotides** varying in length from 20- to 33-mer, and are, therefore, not sequence specific but a property of this chemical structure.
- L58 ANSWER 99 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:139337 HCAPLUS
DN 122:81872
TI Large-scale synthesis, purification, and analysis of **oligodeoxynucleotide phosphorothioates**
AU Padmapriya, A. A.; Tang, Jinyan; **Agrawal, Sudhir**
CS **Hybridon, Inc., Worcester, MA, 01605, USA**
SO Antisense Research and Development (1994), 4(3), 185-99
CODEN: AREDEI; ISSN: 1050-5261
DT Journal
LA English
AB Synthesis of **oligonucleotides** has been carried out on 1-, 2-, and 5-mmole scales using an appropriately modified automated, com. available DNA synthesizer. The reaction cycles were optimized to obtain efficient coupling ($\geq 97\%$). The synthesized **oligonucleotides** were purified by preparative reversed-phase liquid chromatog., followed by detritylation and desalting to obtain the **oligonucleotides** in the Na⁺ form. The purified **oligonucleotides** were characterized by ³¹P NMR, mass spectrometry, capillary gel electrophoresis, and ion-exchange high-performance liquid chromatog. By using these protocols, the 25-mer **oligodeoxyribonucleotide** GEM91 was synthesized on a 1-, 2-, or 5-mmole scale to obtain approx. 2.4, 4.8, or 12 g of purified product.
- L58 ANSWER 100 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:8355 HCAPLUS
DN 122:122408
TI Cellular uptake of **oligodeoxynucleotide phosphorothioates** and their analogs
AU Temsamani, Jamal; Kubert, Michael; Tang, Jinyan; Padmapriya, Abeysinghe; **Agrawal, Sudhir**
CS **Hybridon Inc., Worcester, MA, 01605, USA**
SO Antisense Research and Development (1994), 4(1), 35-42
CODEN: AREDEI; ISSN: 1050-5261
DT Journal
LA English
AB The uptake and intracellular distribution of **oligonucleotide phosphorothioates** (S-oligonucleotides) and their analogs

by various cells lines were studied using internally 35S-labeled **oligonucleotides**. Intracellular accumulation starts in the first 2 h and reaches a maximum at .apprx.16 h. A decrease of intracellular concentration of the S-**oligonucleotide** was observed after 16 h, probably due to a significant efflux transport. Cellular uptake was dependent on the extracellular concentration. The intracellular concentration was significantly higher than that in the medium. The uptake and the intracellular distribution were different in the various cell lines studied. Comparative studies of the uptake of the S-**oligonucleotides** and various 3' end-modified S-**oligonucleotides** show that end modified S-**oligonucleotides** with a hydrophobic group significantly increases the uptake. The introduction of **methylphosphonothioate** linkages at the 3' end of the S-**oligonucleotide** also resulted in an increase in uptake.

L58 ANSWER 101 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:673842 HCAPLUS

DN 121:273842

TI Foldback triplex-forming **oligonucleotides** for use in the regulation of gene expression

IN Kandimalla, Ekambar R.; Agrawal, Sudhir

PA Hybridon Inc., USA

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9417091	A2	19940804	WO 1994-US755	19940121 <--
	WO 9417091	A3	19940915		
	W:	AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN			
	RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	CA 2154358	AA	19940804	CA 1994-2154358	19940121 <--
	AU 9461259	A1	19940815	AU 1994-61259	19940121 <--
	AU 684748	B2	19980108		
	EP 680489	A1	19951108	EP 1994-907851	19940121 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
	CN 1122138	A	19960508	CN 1994-191214	19940121 <--
	JP 08505778	T2	19960625	JP 1994-517202	19940121 <--
	US 5739308	A	19980414	US 1995-418123	19950406 <--
	FI 9503510	A	19950824	FI 1995-3510	19950720 <--
PRAI	US 1993-8000	A2	19930121 <--		
	WO 1994-US755	W	19940121 <--		
	US 1994-248636	B1	19940524 <--		

AB Novel **oligonucleotides** that form a duplex with a target **nucleic acid** and then fold back to form a triplex with the duplex formed between the **oligonucleotide** and the target **nucleic acid** are described as agents for regulating of gene expression using a combination of antisense and antigene approaches. A number of these **oligonucleotides** were synthesized and their properties tested. The **oligonucleotides** were able to form foldback complexes under physiol. conditions with the complexes showing greater stability than either antisense or triple-helix forming mols. alone.

L58 ANSWER 102 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:645487 HCAPLUS

DN 121:245487

TI **Antisense oligodeoxynucleotide phosphorothioate**
complementary to Gag mRNA blocks replication of human immunodeficiency
virus type 1 in human peripheral blood cells

AU Lisziewicz, Julianna; Sun, Daisy; Weichold, Frank F.; Thierry, Alain R.;
Lusso, Paolo; Tang, Jinyan; Gallo, Robert C.; **Agrawal, Sudhir**

CS Lab. Tumor Cell Biology, Natl. Cancer Inst., Bethesda, MD, 20892, USA

SO Proceedings of the National Academy of Sciences of the United States of
America (1994), 91(17), 7942-6

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB Gene-expression modulator 91 (GEM91) is a 25-nt antisense
oligodeoxynucleotide phosphorothioate complementary to
the Gag mRNA of human immunodeficiency virus type 1 (HIV-1). Cellular
uptake and intracellular distribution of GEM91 within cells suggest that
this oligomer is readily available for antisense activity. GEM91
inhibited HIV-1 replication in a dose-dependent and sequence-specific
manner. In a comparative study, 2 μ M GEM91 was as effective as 5 μ M
3'-azido-3'-deoxythymidine in blocking virus replication during the 28-day
treatment of an HIV-1-infected T-cell line. GEM91 also completely
inhibited (>99%) of the growth of three different HIV-1 isolates in
primary lymphocytes and prevented the cytopathic effect of the virus in
primary CD4+ T cells. Similarly, treatment with GEM91 for 3 wk of
HIV-1/BaL-infected primary macrophages blocked virus replication. Based
on GEM91 anti-HIV-activity, safety, and pharmacokinetic profile in
animals, a clin. trial was started using this compound as an antisense
oligonucleotide drug for the treatment of the acquired
immunodeficiency syndrome.

L58 ANSWER 103 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:524614 HCAPLUS

DN 121:124614

TI effect on embryos of injection of **phosphorothioate**-modified
oligonucleotides into pregnant mice

AU Gaudette, Michelle F.; Hampikian, Gregory; Metelev, Valeri; **Agrawal,**
Sudhir; Crain, William R.

CS Cell Biology Group, Worcester Foundat. Exp. Biol., Shrewsbury, MA, 01545,
USA

SO Antisense Research and Development (1993), 3(4), 391-7

CODEN: AREDEI; ISSN: 1050-5261

DT Journal

LA English

AB **Phosphorothioate**-modified **oligonucleotides** were
injected into pregnant female mice to assess the effect on developing
embryos. Injections were carried out during two different time periods,
one when embryos were in preimplantation stages of development (about 3.5
days of development) and the other after implantation, when both a fetus
and placenta are present (from days 9.5 to 11.5 of development). Three
different **phosphorothioate**-modified **oligonucleotides**
were injected. One, which had a sequence not present in the mouse genome,
was used to ask whether nonspecific toxic or teratogenic effects on
embryos result from treatment of the mother. A second was complementary
to the mRNA of the testis-determining factor gene Sry and was used to ask
whether a specific developmental pathway (i.e., sex determination) could be
disrupted in embryos in vivo. The third was the complement of the
anti-Sry sequence. None of these **oligonucleotides** reduced the
frequency of successful pregnancy after mating or the average litter size from
that observed in controls animals. Furthermore, examination of 291 pups or
fetuses from all **oligonucleotide**-injected pregnant females
revealed no developmental defects regardless of which sequence was used.
It is concluded that injection of **phosphorothioate**-modified
oligonucleotides into pregnant females according to the protocols

described here is not toxic or teratogenic to embryos in a nonspecific way. Also, anti-Sry **oligonucleotides** did not influence sex determination in embryos, although there are several possible explanations for this.

L58 ANSWER 104 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:501227 HCAPLUS
 DN 121:101227
 TI Therapeutic anti-HIV **oligonucleotide** and pharmaceutical
 IN Agrawal, Sudhir; Tang, Jin Yan
 PA Hybridon, Inc., USA
 SO PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9408004	A1	19940414	WO 1993-US9392	19931004 <--
	W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, LV, NO, NZ, PL, RO, RU, SD, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, PT, SE				
	EP 664833	A1	19950802	EP 1993-924289	19931004 <--
	EP 664833	B1	19961227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	HU 72400	A2	19960429	HU 1995-995	19931004 <--
	JP 08504570	T2	19960521	JP 1993-509354	19931004 <--
	AT 146819	E	19970115	AT 1993-924289	19931004 <--
	ES 2096343	T3	19970301	ES 1993-924289	19931004 <--
	AU 678415	B2	19970529	AU 1994-54028	19931004 <--
	AU 9454028	A1	19940426		
	BR 9307191	A	19990330	BR 1993-7191	19931004 <--
	US 5684147	A	19971104	US 1994-319823	19941007 <--
	FI 9501600	A	19950510	FI 1995-1600	19950404 <--
	NO 9501307	A	19950601	NO 1995-1307	19950404 <--
PRAI	US 1992-958135	A	19921005 <--		
	WO 1993-US9392	W	19931004 <--		

AB Disclosed are **oligonucleotides** having nucleotide sequences that hybridize to at least **nucleotides** 324 to 348 of a conserved gag region of the HIV-1 genome. These **oligonucleotides** have about 25 to 30 **nucleotides** linked by at least one non-phosphodiester internucleotide linkage which render them resistant to nuclease digestion. Also disclosed are therapeutic formulations containing such **oligonucleotides** and methods of inhibition HIV-1 proliferation and of treating HIV-1 infection in a mammal. **Phosphorothioate-modified oligodeoxynucleotides** 25-30 **nucleotide** in length which hybridize to the specified region of the HIV-1 genome were shown to be more effective than a 20-mer complementary to 327-346 or a 28-mer complementary to only a fragment of the 324-348 region. Syncytia formation, p24 expression, cytopathic effect, and reverse transcriptase activity were monitored to assay the effects of the antisense **oligonucleotides**.

L58 ANSWER 105 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:449554 HCAPLUS
 DN 121:49554
 TI Pharmacokinetics, biodistribution, and stability of capped **oligodeoxynucleotide phosphorothioates** in mice
 AU Temsamani, Jamal; Tang, Jin Yan; Padmapriya, Abeysinghe; Kubert, Michael; Agrawal, Sudhir
 CS Hybridon, Inc., Worcester, MA, 01605, USA
 SO Antisense Res. Dev. (1993), 3(3), 277-84
 CODEN: AREDEI; ISSN: 1050-5261

DT Journal
 LA English
 AB Several end-modified **oligodeoxynucleotide phosphorothioates** (S-oligonucleotides) were studied for their pharmacokinetics, biodistribution, excretion, and metabolic stability in vivo after i.v. administration to mice. The overall tissue distribution and excretion patterns of these S-oligonucleotides were independent of the 5' or 3' end modification studied. However, the 3' end modification proved to be of considerable importance with respect to the metabolic stability of the **oligonucleotides**. In the case of uncapped and 5'-capped S-oligonucleotides, only 50% of the substances was recovered intact from liver and kidneys out of the total bioavailable concentration. In contrast, almost all the bioavailable concns. of 3'-capped **oligonucleotide** were intact in the kidneys and liver 24 h after administration. These results demonstrate that superior pharmaceutical potentials can be created by 3' end modification of **oligonucleotide phosphorothioates**.

L58 ANSWER 106 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:144158 HCAPLUS
 DN 120:144158
 TI Nuclease-resistant **oligonucleotides** stabilized by internal hybridization and their use as therapeutic agents
 IN Agrawal, Sudhir; Tang, Jin Yan
 PA Hybridon, Inc., USA
 SO PCT Int. Appl., 48 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9401550	A1	19940120	WO 1993-US6326	19930702	<--
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, RO, RU, SD, SE, SK, UA, US, VN					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9347700	A1	19940131	AU 1993-47700	19930702	<--
	EP 649467	A1	19950426	EP 1993-918146	19930702	<--
	EP 649467	B1	19980916			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	HU 69981	A2	19950928	HU 1994-3788	19930702	<--
	JP 08501928	T2	19960305	JP 1993-503450	19930702	<--
	PL 172710	B1	19971128	PL 1993-307025	19930702	<--
	AT 171210	E	19981015	AT 1993-918146	19930702	<--
	NO 9405020	A	19950228	NO 1994-5020	19941223	<--
	FI 9406201	A	19941230	FI 1994-6201	19941230	<--
PRAI	US 1992-909069		19920702			<--
	WO 1993-US6326		19930702			<--

AB Improved antisense **oligonucleotides** that are resistant to nucleolytic degradation have two regions: a target hybridizing region complementary to a nucleic acid sequence that is from a pathogen, or a cellular gene; and a self-complementary region. Such **oligonucleotides** are called self-stabilized **oligonucleotides**. The nuclease resistance of these **oligonucleotides** may be increased by using unusual bondings such as **phosphorothioates**. An **oligonucleotide** complementary to the gag gene of HIV-1 was digested by snake venom **phosphodiesterase** with a half-life of 75 s; a self-stabilized **oligonucleotide** carrying a 3' tail of 10 self-complementary **oligonucleotides** had a half-life of 950 s under the same conditions. The nuclease resistance of these **oligonucleotides**

was greatly increased in the **phosphorothioate** analog; the half-life of the analog of the first **oligonucleotides** was increased to 4 h and the analog of the second was essentially undegraded after 4 h. The self-stabilized **oligonucleotide** was an effective inhibitor of HIV-1 growth in H9 lymphocytes, as judged by inhibition of p24 synthesis, with an IC₅₀ of 0.25-0.35 µg/mL, compared to 2-2.8 µg/mL for the non-stabilized **oligonucleotide**.

L58 ANSWER 107 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:123952 HCAPLUS

DN 120:123952

TI A rapid method for quantitation of **oligodeoxynucleotide phosphorothioates** in biological fluids and tissues

AU Temsamani, Jamal; Kubert, Michael; Agrawal, Sudhir

CS Hybridon, Inc., Worcester, MA, 01605, USA

SO Analytical Biochemistry (1993), 215(1), 54-8

CODEN: ANBCA2; ISSN: 0003-2697

DT Journal

LA English

AB The method is based on the extraction of the **oligonucleotide** from the biol. fluids and tissues and immobilization on a nylon membrane. The membrane-bound **oligodeoxynucleotide phosphorothioate** is then hybridized with labeled complementary **oligonucleotide** and exposed to x-ray film. The data on the film can be scanned and used to create a standard curve. The sensitivity of detection by the method described here will be useful to monitor the pharmacokinetics of **oligonucleotides** in bodily fluids and distribution in various tissues. The results indicate that the method is rapid and allows handling of a large number of samples at the same time.

L58 ANSWER 108 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:640937 HCAPLUS

DN 119:240937

TI Self-stabilized antisense **oligodeoxynucleotide phosphorothioates**: Properties and anti-HIV activity

AU Tang, Jin Yan; Temsamani, Jamal; Agrawal, Sudhir

CS Hybridon, Inc., Worcester, MA, 01605, USA

SO Nucleic Acids Research (1993), 21(11), 2729-35

CODEN: NARHAD; ISSN: 0305-1048

DT Journal

LA English

AB A new class of **oligodeoxyribonucleotides** has been designed, referred to here as 'self-stabilized' **oligonucleotides**. These **oligonucleotides** have hairpin loop structures at their 3' ends, and show increased resistance to degradation by snake venom phosphodiesterase, DNA polymerase I and fetal bovine serum. The self-stabilized region of the **oligonucleotide** does not interfere in hybridization with complementary **nucleic acids** as shown by melting temperature, mobility-shift and RNase H cleavage studies. Various self-stabilized **oligonucleotides** containing increasingly stable hairpin loop regions were studied for their anti-HIV activity. Pharmacokinetic and stability studies in mice showed increased in vivo persistence of self-stabilized **oligonucleotides** with respect to their linear counterparts.

L58 ANSWER 109 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:616665 HCAPLUS

DN 119:216665

TI Quantitative analysis of **phosphorothioate oligonucleotides** in biological fluids using fast anion-exchange chromatography

AU Bourque, A. J.; Cohen, A. S.

CS Hybridon, Inc., Worcester, MA, 01605, USA

SO Journal of Chromatography, Biomedical Applications (1993),

617(1), 43-4.

CODEN: JCBADL; ISSN: 0378-4347

DT Journal

LA English

AB **Phosphorothioate oligonucleotides** are potentially useful as antiviral drugs. Classical DNA extraction methods are not as effective on short single-stranded DNA as with longer double-stranded chains. The classical method of phenol-chloroform extraction followed by ethanol precipitation is difficult to quantify, thus monitoring of the pharmacol.

disposition of these compds. is subject to error. A method was devised and validated for extraction and anal. of modified **oligonucleotides** from biol. fluids such as urine and serum based on protein kinase digestion and phenol-chloroform extraction. Due to the high native UV absorbance of the oligomers, detection limits in the low ppb range were obtained without derivatization.

L58 ANSWER 110 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:574882 HCAPLUS

DN 119:174882

TI Method for sequencing synthetic **oligodeoxynucleotide phosphorothioates**

AU Tang, Jinyan; Roskey, Allysen M.; Agrawal, Sudhir

CS Hybridon, Inc., Worcester, MA, 01605, USA

SO Analytical Biochemistry (1993), 212(1), 134-7

CODEN: ANBCA2; ISSN: 0003-2697

DT Journal

LA English

AB Sequencing of **oligodeoxynucleotide phosphorothioate** by a modified Sanger method of sequencing is described. The procedure involves ligation of synthetic **oligodeoxynucleotide phosphorothioate** to an **oligodeoxynucleotide**, referred to here as "helper **oligonucleotide**". The helper **oligonucleotide** has a region which is complementary to T7 primer. By using DNA polymerase and a **nucleoside triphosphate** mixture, 5'-labeled T7 primer is extended onto ligated **oligodeoxynucleotide phosphorothioate**, which is then analyzed on gel electrophoresis.

L58 ANSWER 111 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:573628 HCAPLUS

DN 119:173628

TI Long-term treatment of human immunodeficiency virus-infected cells with antisense **oligonucleotide phosphorothioates**

AU Lisziewicz, Julianna; Sun, Daisy; Metelev, Valeri; Zamecnik, Paul; Gallo, Robert C.; Agrawal, Sudhir

CS Lab. Tumor Cell Biol., Natl. Cancer Inst., Bethesda, MD, 20853, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1993), 90(9), 3860-4

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB The antiviral activity of antisense **oligodeoxy-nucleotide phosphorothioates** complementary to the tat gene, the gag mRNA, and the rev mRNA were studied in a long-term infection model. Three antisense **oligonucleotides** directed to the splice-acceptor site of the tat gene failed to suppress human immunodeficiency virus type I replication at 1 μ M concentration in the long-term culture. In contrast, two **oligodeoxynucleotide phosphorothioates** (28-mer) complementary to the gag and the rev mRNAs inhibited viral replication for >80 days, and the antiviral activity was sequence- and length-dependent. In addition, after pretreatment of cells, the authors could reduce the concentration

of the antisense **oligodeoxynucleotides** by >10-fold and still maintain the inhibition of viral replication. These results suggest that chemotherapy for human immunodeficiency virus type 1 infection with antisense **oligodeoxynucleotide phosphorothioates** may be achieved by an initial high-dose treatment followed by a lower maintenance dose.

L58 ANSWER 112 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:573523 HCAPLUS

DN 119:173523

TI Comparison of cellular binding and uptake of antisense **phosphodiester, phosphorothioate, and mixed phosphorothioate and methylphosphonate oligonucleotides**

AU Zhao, Qiuyan; Matson, Sara; Herrera, Charles J.; Fisher, Eric; Yu, Hong; Krieg, Arthur M.

CS Coll. Med., Univ. Iowa, Iowa City, IA, USA

SO Antisense Research and Development (1993), 3(1), 53-66

CODEN: AREDEI; ISSN: 1050-5261

DT Journal

LA English

AB The effects of **phosphorothioate (S-oligonucleotide)** or terminal **phosphorothioate-phosphodiester (S-O-oligonucleotides)** or **methylphosphonate-phosphodiester (MP-O-oligonucleotides)** modifications on mouse spleen cell surface binding, uptake, and degradation were studied using fluorescein (FITC)-conjugated **oligonucleotides**. **S-oligonucleotides** had the highest cell binding and uptake, followed by **S-O-, O-, and MP-O-oligonucleotides**. Competition studies indicated that **S-oligonucleotides** have an increased affinity for cell membrane **oligonucleotide** binding sites, because they could completely block **O-oligonucleotide** binding at a molar ratio of just 0.1. Uptake of all **oligonucleotides** was higher in B cells than T cells and was increased by stimulation with the B-cell mitogen, lipopolysaccharide. Although the authors' cells had been purified using conventional techniques to eliminate dead cells, there remained about 5% of cells that were dead or dying, as determined by flow cytometry using propidium iodide staining. Of note, **oligonucleotide** association with dead cells was approx. 50-fold greater than that with living cells. Confocal microscopy confirmed that the **oligonucleotides** in living cells were intracellular, and indicated little nuclear uptake by 4 h. While extensive degradation of intracellular **O-oligonucleotides** was apparent by 4 h, there was no detectable degradation of **S-, S-O-, or MP-O-oligonucleotides**.

L58 ANSWER 113 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:487501 HCAPLUS

DN 119:87501

TI High-performance liquid chromatography and capillary gel electrophoresis as applied to antisense DNA

AU Cohen, Aharon S.; Vilenchik, Maria; Dudley, Judith L.; Gemborys, Mark W.; Bourque, Andre J.

CS Hybridon Inc., Worcester, MA, 01605, USA

SO Journal of Chromatography (1993), 638(2), 293-301

CODEN: JOCRAM; ISSN: 0021-9673

DT Journal

LA English

AB Reversed-phase and ion-exchange HPLC are compared with both slab gel and capillary gel electrophoresis for the separation of antisense **phosphorothioate** oligomers. The chromatog. sepns. were found to be markedly inferior to the electrophoretic sepns., especially for oligomers greater than 20 bases in length. The potential of gel high-performance capillary electrophoresis for the anal. of **phosphorothioate**

analogs is shown.

L58 ANSWER 114 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:462145 HCAPLUS
 DN 119:62145
 TI GEM 91 - an antisense **oligonucleotide phosphorothioate**
 as a therapeutic agent for AIDS
 AU **Agrawal, Sudhir**; Tang, Jin Yan
 CS **Hybridon, Inc., Worcester, MA, USA**
 SO Antisense Research and Development (1992), 2(4), 261-6
 CODEN: AREDEI; ISSN: 1050-5261
 DT Journal; General Review
 LA English
 AB A review and discussion with 18 refs.

L58 ANSWER 115 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:419978 HCAPLUS
 DN 119:19978
 TI Antimalarial activities of **oligodeoxynucleotide phosphorothioates** in chloroquine-resistant *Plasmodium falciparum*
 AU Rapaport, Eliezer; Misiura, Konrad; **Agrawal, Sudhir**; Zamencnik, Paul
 CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
 SO Proceedings of the National Academy of Sciences of the United States of America (1992), 89(18), 8577-80
 CODEN: PNASA6; ISSN: 0027-8424
 DT Journal
 LA English
 AB Synthetic **oligonucleotides** and their chemical modifications have been shown to inhibit viral and cellular gene expression by sequence-specific antisense hybridization to target mRNAs. **Oligodeoxynucleotide phosphorothioates** and their nuclease-resistant modifications are effective in micromolar and submicromolar concns. against the growth of both chloroquine-resistant and chloroquine-sensitive strains of *Plasmodium falciparum* in vitro. Parasitized human erythrocytes were found to be accessible to radioactively labeled **oligodeoxynucleotides**, whereas the uninfected erythrocytes did not permit any cellular entry of the same compds. The dihydrofolate reductase-thymidylate synthase gene of *P. falciparum* was demonstrated to be a good target for sequence-dependent inhibition of plasmodial growth by exogenously administered modified **oligonucleotides**. The antimalarial activities observed in vitro were identical for chloroquine-sensitive and chloroquine-resistant strains of *P. falciparum*. The antimalarial activity of **oligodeoxynucleotide phosphorothioates** is related to sequence complementarity to certain regions of the plasmodial genome as well as to nonsequence-defined activities.

L58 ANSWER 116 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:251067 HCAPLUS
 DN 118:251067
 TI 3'-end blocked **oligonucleotides**
 IN **Agrawal, Sudhir**; Temsamani, Jamal; Tang, Jin Yan
 PA **Hybridon, Inc., USA**
 SO PCT Int. Appl., 24 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9220697	A1	19921126	WO 1992-US3867	19920508 <--
	W: CA, JP, KR				

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
 CA 2102804 AA 19921111 CA 1992-2102804 19920508 <--
 EP 588881 A1 19940330 EP 1992-912090 19920508 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE
 JP 07501314 T2 19950209 JP 1992-500109 19920508 <--

PRAI US 1991-698568 19910510 <--
 WO 1992-US3867 19920508 <--

AB **Oligonucleotides** are disclosed which have the 3'-end blocked by cap structures and which have ≥ 1 artificial **internucleoside** linkages (**phosphorothioate**, sulfone, **phosphoramidate**, etc.). Such **oligonucleotides** are resistant to in vivo degradation and extension and therefore have superior half-lives in vivo. A **phosphorothioate oligonucleotide** (ACACCCAATTCTGAAAATGG) was synthesized with either no cap, a 3'-cap, a 5'-cap, or with caps at both termini; the cap structure was an OP(:O)(S)OCH₂CH(OH)CH₂NH₂ moiety. Stability of these **oligonucleotide phosphorothioates** (also labeled with 35S) was assessed in monkey plasma. Uncapped and 5'-capped **oligonucleotide phosphorothioates** were degraded extensively within 24 h. In contrast, 3'-capped and 3',5'-capped **oligonucleotide phosphorothioates** were stable after 24 h. The degradation was mediated by 3'-exonuclease activity. Biodistribution data and assessment of stability of the **oligonucleotide phosphorothioates** in organs is also presented.

L58 ANSWER 117 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:116248 HCAPLUS

DN 118:116248

TI Specific inhibition of human immunodeficiency virus type 1 replication by antisense **oligonucleotides**: an in vitro model for treatment

AU Lisziewicz, Julianna; Sun, Daisy; Klotman, Mary; Agrawal, Sudhir; Zamecnik, Paul; Gallo, Robert

CS Lab. Tumor Cell Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1992), 89(23), 11209-13
 CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB We have developed a culture system, simulating in vivo conditions of human immunodeficiency virus type 1 (HIV-1) infection, to evaluate the long-term efficacy of antisense **oligonucleotide** treatment. Five **oligonucleotide phosphorothioates** (28-mers), complementary to different regions of HIV-1 RNA, blocked replication of the virus in a sequence-specific manner at 1 μ M concentration. Variations in antiviral activity were seen among the different **oligonucleotides**, revealing an effect of target selection. Mismatched or random **oligonucleotide phosphorothioates** delayed, but did not completely inhibit, HIV-1 replication. In the case of inhibition by a splice-acceptor-site antisense **oligodeoxynucleotide**, a breakthrough phenomenon occurred after 25 days of treatment, suggesting the development of an "escape mutant". This result did not occur when the inhibitory **oligodeoxynucleotides** were complementary to the primary-sequence areas of the rev-responsive element and rev-1 genes. Sequential treatment of HIV-1-infected cells with a combination of different antisense **oligonucleotides**, each administered once, also prevented the development of escape mutants. Results suggest that chemotherapy based on specifically targeted antisense-**oligonucleotide phosphorothioates** may be an effective method for reducing the viral burden in HIV-1-infected individuals at clin. achievable **oligonucleotide** concns.

L58 ANSWER 118 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

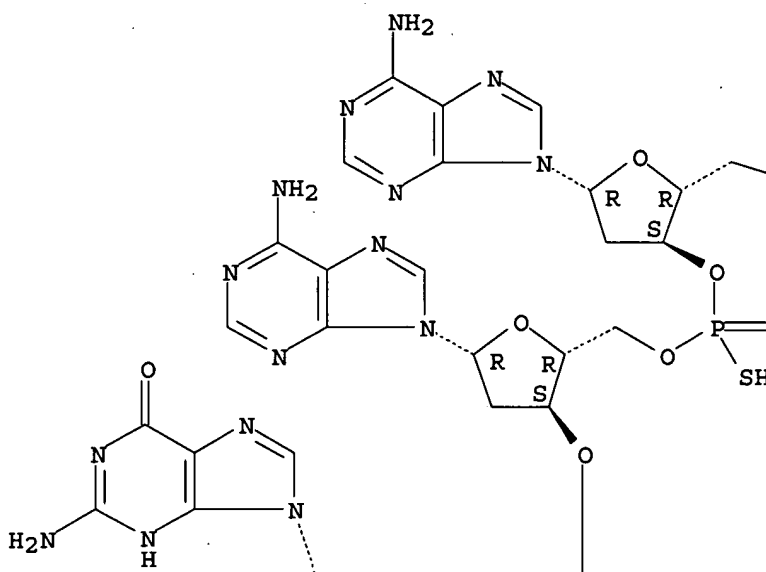
AN 1992:169299 HCAPLUS

DN 116:169299

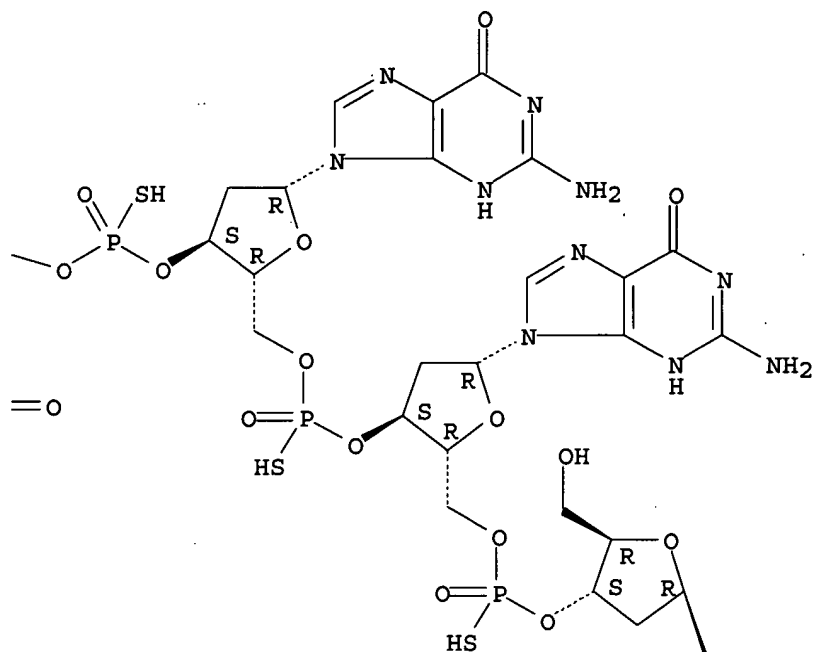
TI Ion-exchange high-performance liquid chromatography analysis of
oligodeoxyribonucleotide phosphorothioates
 AU Metelev, Valeri; Agrawal, Sudhir
 CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
 SO Analytical Biochemistry (1992), 200(2), 342-6
 CODEN: ANBCA2; ISSN: 0003-2697
 DT Journal
 LA English
 AB To analyze and purify **oligonucleotide** analogs, HPLC using a weak
 anion-exchange column is described. The separation of **oligonucleotide**
phosphorothioates is found to be length dependent.
 IT 139730-29-3
 RL: ANT (Analyte); ANST (Analytical study)
 (separation of, by anion-exchange HPLC)
 RN 139730-29-3 HCAPLUS
 CN Guanosine, P-thiothymidylyl-(5'→3')-P-thiothymidylyl-(5'→3')-
 P-thiothymidylyl-(5'→3')-2'-deoxy-P-thiocytidylyl-(5'→3')-2'-
 deoxy-P-thioguananylyl-(5'→3')-2'-deoxy-P-thioadenylyl-(5'→3')-
 2'-deoxy-P-thioadenylyl-(5'→3')-2'-deoxy-P-thioguananylyl-
 (5'→3')-2'-deoxy-P-thioguananylyl-(5'→3')-2'-deoxy- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

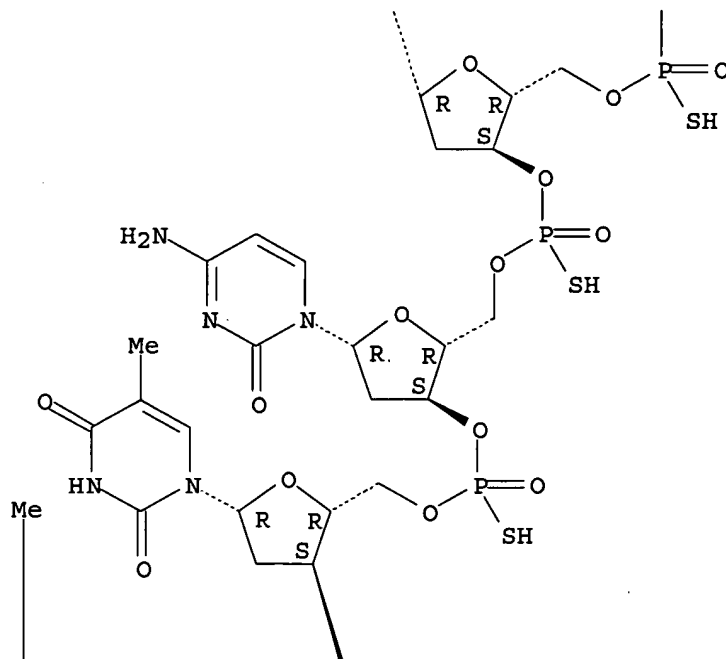
PAGE 1-A



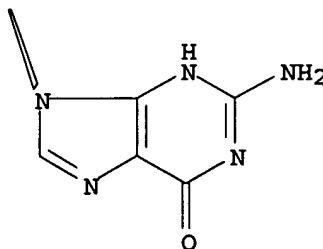
PAGE 1-B



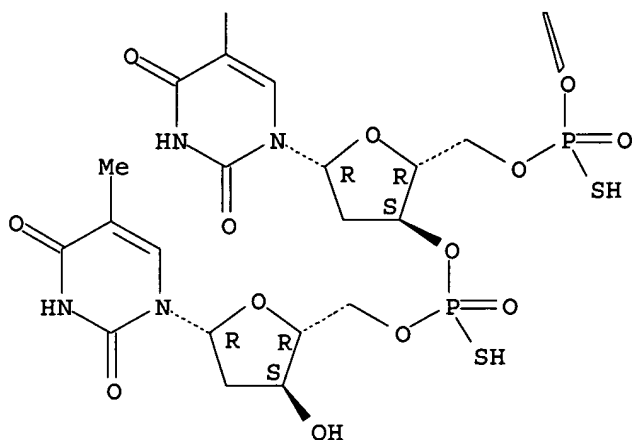
PAGE 2-A



PAGE 2-B



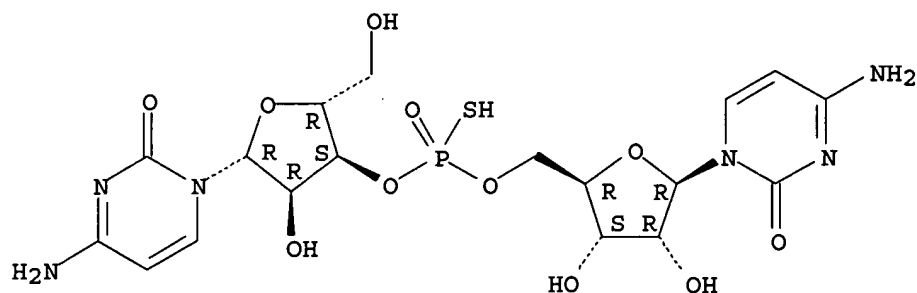
PAGE 3-A



L58 ANSWER 119 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:622676 HCAPLUS
 DN 115:222676
 TI Pharmacokinetics, biodistribution, and stability of
oligodeoxynucleotide phosphorothioates in mice
 AU Agrawal, Sudhir; Temsamani, Jamal; Tang, Jin Yan
 CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
 SO Proceedings of the National Academy of Sciences of the United States of
 America (1991), 88(17), 7595-9
 CODEN: PNASA6; ISSN: 0027-8424
 DT Journal
 LA English
 AB Studies of the pharmacokinetics, biodistribution, and excretion of an
oligodeoxynucleotide phosphorothioate ([S]
oligonucleotide) in mice are described. The [S]
oligonucleotide used had the base sequence 5'-ACA-CCC-AAT-TCT-GAA-
 AAT-GG-3', which is complementary to the HIV tat splice acceptor site.
 After either i.v. or i.p. administration of a single dose (30 mg/kg), [S]
oligonucleotide (35S-labeled at each **internucleotide**
 linkage) was found in most of the tissues for ≤ 48 h. About 30% of
 the dose was excreted in urine within 24 h, irrespectively of the mode of
 administration; the excreted [S]**oligonucleotide** was extensively
 degraded. In plasma, stomach, heart, and intestines, the [S]
oligonucleotide was degraded by only 15%, whereas in the kidneys
 and liver, degradation was approx. 50% in 48 h. The surprising observation was
 made that chain length extension of administered [S]
oligonucleotide occurred in kidneys, liver, and intestines.

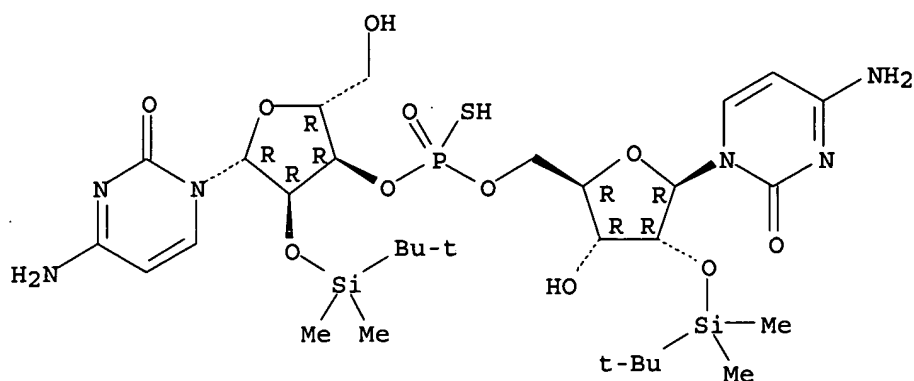
L58 ANSWER 120 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:143880 HCAPLUS
 DN 114:143880
 TI Efficient synthesis of oligoribonucleotide and its phosphorothioate analog using H-phosphonate approach
 AU Agrawal, Sudhir; Tang, J. Y.
 CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
 SO Tetrahedron Letters (1990), 31(52), 7541-4
 CODEN: TELEAY; ISSN: 0040-4039
 DT Journal
 LA English
 AB Efficient solid phase synthesis of oligoribonucleotide and its phosphorothioate analog is described that utilizes the dimethoxytrityl (DMTr) for 5'-protection and t-butyldimethylsilyl (t-BDMS) group for 2'-protection of ribonucleoside monomers and the H-phosphonate coupling procedure. The synthetic cycles were optimized to use only 8-10 fold excess of monomer at each coupling step, leading to an average coupling yield of 97%.
 IT 132696-48-1
 RL: PROC (Process)
 (HPLC and phosphorus-31 NMR of)
 RN 132696-48-1 HCAPLUS
 CN Cytidine, P-thiocytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 132606-91-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and desilylation of, kinetics of)
 RN 132606-91-8 HCAPLUS
 CN Cytidine, 2'-O-[(1,1-dimethylethyl)dimethylsilyl]-P-thiocytidylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



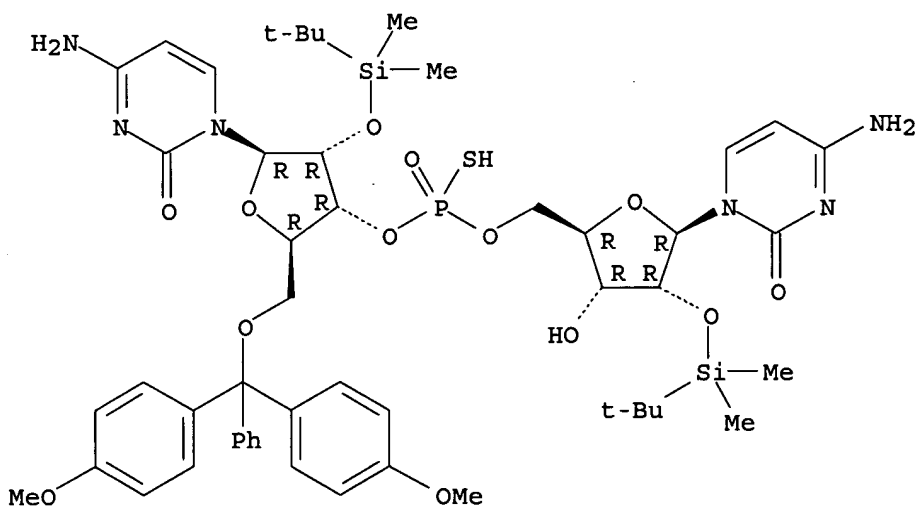
IT 132606-92-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and detritylation of, kinetics of)

RN 132606-92-9 HCAPLUS

CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-[(1,1-dimethylethyl)dimethylsilyl]-P-thiocytidylyl-(3'→5')-2'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L58 ANSWER 121 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:528809 HCAPLUS

DN 113:128809

TI Analytical study of **phosphorothioate** analogs of **oligodeoxynucleotides** using high-performance liquid chromatography

AU **Agrawal, Sudhir**; Tang, J. Y.; Brown, D. M.

CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA

SO Journal of Chromatography (1990), 509(2), 396-9

CODEN: JOCRAM; ISSN: 0021-9673

DT Journal

LA English

AB **Phosphorothioate oligodeoxyribonucleotides** were purified by reversed-phase and ion-exchange HPLC.

IT 129318-51-0

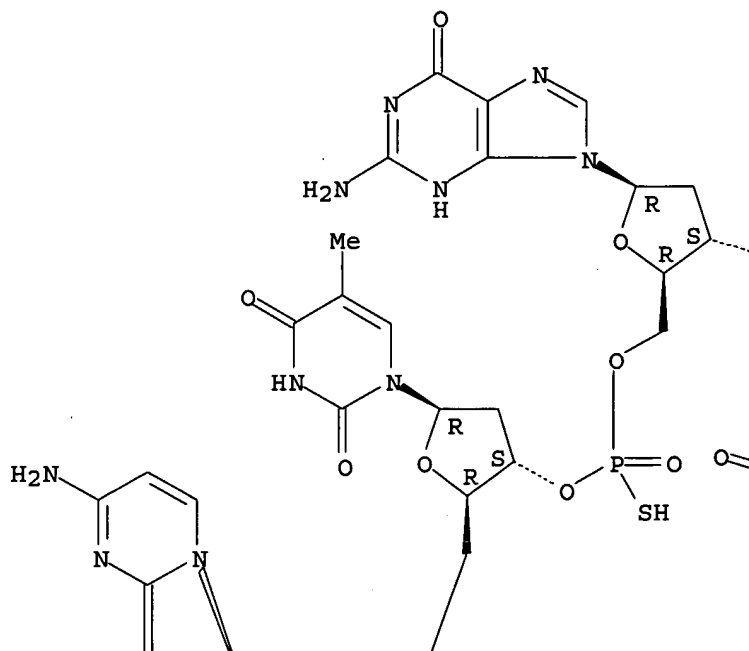
RL: ANT (Analyte); ANST (Analytical study)
(anal. of, by HPLC)

RN 129318-51-0 HCAPLUS

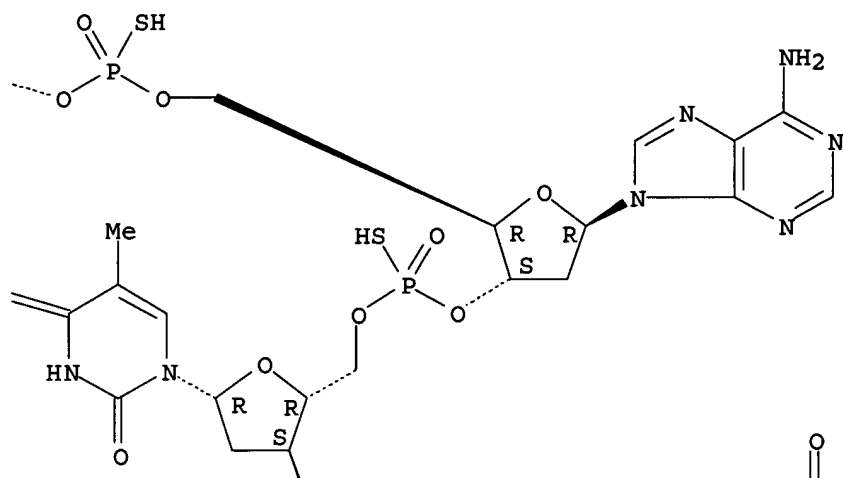
CN Cytidine, 2'-deoxy-P-thioadenylyl-(3'→5')-2'-deoxy-P-thiocytidylyl-
(3'→5')-P-thiothymidylyl-(3'→5')-2'-deoxy-P-thioguanynylyl-
(3'→5')-2'-deoxy-P-thioadenylyl-(3'→5')-P-thiothymidylyl-
(3'→5')-2'-deoxy-P-thioguanynylyl-(3'→5')-2'-deoxy- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

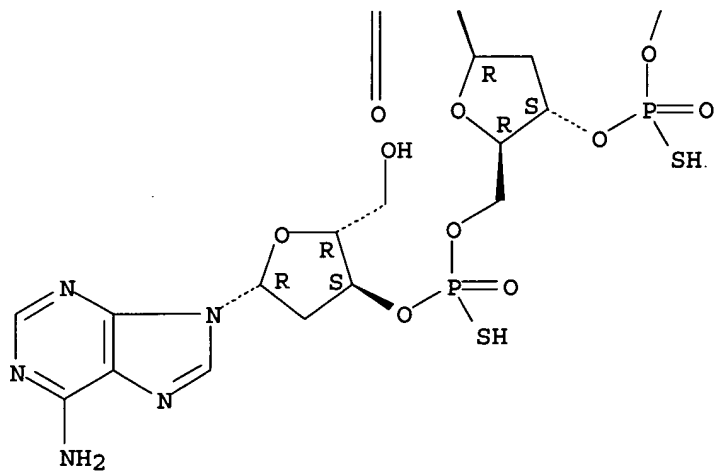
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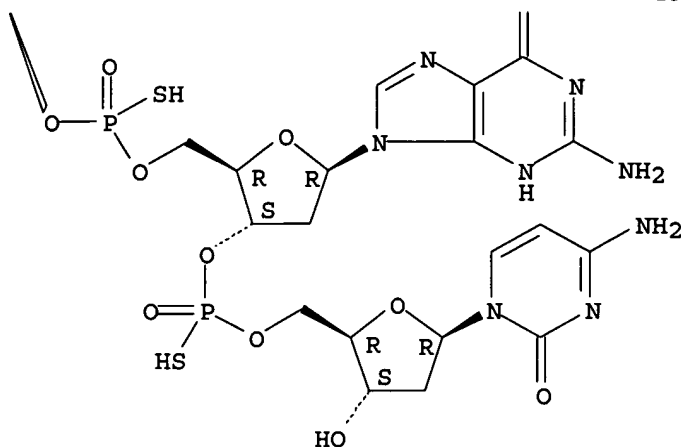
PAGE 1-B



PAGE 2-A



PAGE 2-B



L58 ANSWER 122 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:434393 HCAPLUS
 DN 113:34393
 TI Inhibition of influenza virus replication by **phosphorothioate oligodeoxynucleotides**
 AU Leiter, Josef M.; Agrawal, Sudhir; Palese, Peter; Zamecnik, Paul C.
 CS Dep. Microbiol., Mount Sinai Sch. Med., New York, NY, 10029, USA
 SO Proceedings of the National Academy of Sciences of the United States of America (1990), 87(9), 3430-4
 CODEN: PNASA6; ISSN: 0027-8424
 DT Journal
 LA English
 AB **Oligodeoxynucleotides** (ODNs) were synthesized and tested for their antiviral activity against influenza viruses. ODNs corresponded to the polymerase PB1 gene of either influenza A/WSN/33 virus or influenza C/JJ/50 virus. All compds. were 20 **nucleotides** long, including control ODNs containing mismatches. The **phosphodiester** ODNs (O-ODNs) failed to inhibit replication of influenza A and influenza C viruses at concns. up to 80 μ M, possibly due to intracellular nuclease digestion of the unmodified oligomers. By contrast, the **phosphorothioate** derivs. (S-ODNs) inhibited replication of both influenza A and influenza C virus. The antiviral effect of S-ODNs against influenza A virus was found at concns. as low as 1.25 μ M and was present with mismatched oligomers. In the case of influenza C virus, the S-ODN complementary to the 3' end of the viral RNA of the PB1 gene revealed a sequence-specific antiviral activity at a concentration of 20 μ M. (At the same concentration, S-ODNs with one or three mismatches showed little or no antiviral activity.). Reduction in plaque number reached six logarithms when this sequence-specific S-ODN was used at a concentration of 80 μ M.

L58 ANSWER 123 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:30348 HCAPLUS
 DN 112:30348
 TI Inhibition of human immunodeficiency virus in early infected and chronically infected cells by antisense **oligodeoxynucleotides** and their **phosphorothioate** analogs
 AU Agrawal, Sudhir; Ikeuchi, Tohru; Sun, Daisy; Sarin, Prem S.; Konopka, Andrzej; Maizel, Jacob; Zamecnik, Paul C.
 CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA

- SO Proceedings of the National Academy of Sciences of the United States of America (1989), 86(20), 7790-4
CODEN: PNASA6; ISSN: 0027-8424
- DT Journal
LA English
AB Antisense **oligodeoxynucleotides**, both the **phosphorothioate** analogs and unmodified oligomers of the same sequence, inhibit replication and expression of human immunodeficiency virus already growing in tissue cultures of MOLT-3 cells with much greater efficacy than do mismatched (random) oligomers and homooligomers of the same length and with the same **internucleotide** modification. This preferential inhibitory effect is elicited in as short a time as 4-24 h postinfection. Likewise, antisense oligomers exhibit greater inhibitory effects on human immunodeficiency virus in chronically infected cells than do mismatched oligomers and homooligomers. **Phosphorothioate** antisense oligomers are up to 100-fold more potent than unmodified oligomers of the same sequence in these inhibitory assays. These results, in major respects, confirm and extend those recently published by M. Matsukura et al. (1989). They also point out the importance of computer anal. of sequences thought to be random but that in reality contain significant areas of likely hybridization, either to the viral genome or to the cDNA strand synthesized from it. They thus reinforce the concept that specific base pairing is a crucial feature of **oligonucleotide** inhibition of human immunodeficiency virus.
- L58 ANSWER 124 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:185365 HCAPLUS
DN 110:185365
TI **Oligodeoxynucleotide phosphoramidates** and **phosphorothioates** as inhibitors of human immunodeficiency virus [Erratum to document cited in CA110(1):267g]
AU Agrawal, Sudhir; Goodchild, John; Civeira, Maria P.; Thornton, Arthur H.; Sarin, Prem S.; Zamecnik, Paul C.
CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1989), 86(5), 1504
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB An error in the text has been corrected The error was not reflected in the abstract or the index entries.
- L58 ANSWER 125 OF 125 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:267 HCAPLUS
DN 110:267
TI **Oligodeoxynucleotide phosphoramidates** and **phosphorothioates** as inhibitors of human immunodeficiency virus
AU Agrawal, Sudhir; Goodchild, John; Civeira, Maria P.; Thornton, Arthur H.; Sarin, Prem S.; Zamecnik, Paul C.
CS Worcester Found. Exp. Biol., Shrewsbury, MA, 01545, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1988), 85(19), 7079-83
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Modified **oligodeoxynucleotides** complementary to RNA of human immunodeficiency virus 1 (HIV-1) were prepared and tested for their ability to inhibit virally induced syncytium formation and expression of viral p24 protein. The modifications of oligomers include replacement of backbone **phosphodiester** groups with **phosphorothioates** and 3 **phosphoramidates** (butylamidate, piperazidate, morpholidate). All oligomers were active. Oligomers with complete replacement of **phosphodiester**s with **phosphoramidate** or

phosphorothioate groups were more active at micromolar concns. than were unmodified oligomers of the same sequence. In addition, modified and unmodified **homooligonucleotides** also showed inhibition of HIV-1 replication. Different classes of **oligonucleotides** may inhibit HIV replication by different mechanisms.

=> => fil biosis

FILE 'BIOSIS' ENTERED AT 06:35:32 ON 29 JUN 2004

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RECORDS LAST ADDED: 23 June 2004 (20040623/ED)

FILE RELOADED: 19 October 2003.

=> d all tot

L81 ANSWER 1 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1999:170452 BIOSIS

DN PREV199900170452

TI **Antisense therapeutics: Beyond phosphorothioate oligodeoxynucleotides.**

AU **Agrawal, Sudhir** [Reprint author]

CS **Hybridon Inc., Milford, MA 01757, USA**

SO **Abstracts of Papers American Chemical Society, (1999) Vol. 217, No. 1-2, pp. CARB 10. print.**

Meeting Info.: **217th National Meeting of the American Chemical Society, Anaheim, California, USA. March 21-25, 1999. American Chemical Society.**

CODEN: ACSRAL. ISSN: 0065-7727.

DT **Conference; (Meeting)**

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 19 Apr 1999

Last Updated on STN: 19 Apr 1999

CC Pharmacology - General 22002

Biochemistry methods - General 10050

Biochemistry studies - General 10060

General biology - Symposia, transactions and proceedings 00520

IT Major Concepts

Methods and Techniques; Pharmacology

IT Chemicals & Biochemicals

phosphorothioate oligodeoxynucleotides:

antisense therapeutics, synthesis, pharmaceutical

IT Methods & Equipment

pharmaceutical synthesis: synthetic method

IT Miscellaneous Descriptors

Meeting Abstract

RN 15181-41-6 (PHOSPHOROTHIOATE)

L81 ANSWER 2 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1998:337777 BIOSIS

DN PREV199800337777

TI **Studies of a hybrid oligonucleotide for antisense imaging.**

AU **Rusckowski, M.; Qu, T.; Hnatowich, D. J.; Agrawal, S.**

CS **Univ. Mass. Med. Center, Worcester, MA, USA**

SO **Journal of Nuclear Medicine, (May, 1998) Vol. 39, No. 5 SUPPL., pp. 219P. print.**

Meeting Info.: **45th Annual Meeting of the Society of Nuclear Medicine.** Toronto, Ontario, Canada. June 7-11, 1998. Society of Nuclear Medicine.

CODEN: JNMEAQ. ISSN: 0161-5505.

DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LA English

ED Entered STN: 12 Aug 1998

Last Updated on STN: 10 Sep 1998

CC Neoplasms - General 24002
 Cytology - General 02502
 Radiation biology - General 06502
 Biochemistry studies - General 10060
 Pharmacology - General 22002
General biology - Symposia, transactions and proceedings 00520

IT Major Concepts

Pharmacology; Tumor Biology

IT Chemicals & Biochemicals

oligonucleotides; phosphorothioate DNA;

technetium-99m mercaptoacetyltriserine

IT Miscellaneous Descriptors

Meeting Abstract; Meeting Poster

ORGN Classifier

Animalia 33000

Super Taxa

Animalia

Organism Name

LS174T: tumor cells

Taxa Notes

Animals

ORGN Classifier

Muridae 86375

Super Taxa

Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

mouse: nude

Taxa Notes

Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates

L81 ANSWER 3 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1998:104987 BIOSIS

DN PREV199800104987

TI Retinal uptake, autoradiography and metabolic profiling of GEM 132 in male Dutch belted rabbits and rhesus monkeys after a single intravitreal injection of 14C or 35S-GEM 132.

AU Dvorchik, Barry H. [Reprint author]; Grindel, J. Michael [Reprint author]; Ferdinandi, Eckhardt S.

CS Hybridon Inc., Cambridge, MA 02139, USA

SO Pharmaceutical Research (New York), (Nov., 1997) Vol. 14, No. 11 SUPPL., pp. S330. print.

Meeting Info.: **Annual Meeting of the American Association of Pharmaceutical Scientists.** Boston, Massachusetts, USA. November 2-6, 1997. American Association of Pharmaceutical Scientists.

CODEN: PHREEB. ISSN: 0724-8741.

DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LA English

ED Entered STN: 3 Mar 1998

Last Updated on STN: 3 Mar 1998

CC Chemotherapy - Antiviral agents 38506

Radiation biology - Radiation and isotope techniques 06504
 Pharmacology - Drug metabolism and metabolic stimulators 22003
General biology - Symposia, transactions and proceedings 00520
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Virology - Animal host viruses 33506

IT Major Concepts

Pharmacology

IT Chemicals & Biochemicals

GEM 132: **antisense** hybrid **phosphorothioate**
oligonucleotide, antiviral agent, retinal uptake, carbon-14
 labeled, sulfur-35 labeled

IT Methods & Equipment

autoradiography

IT Miscellaneous Descriptors

pharmacokinetics; **Meeting Abstract; Meeting Poster**

ORGN Classifier

Cercopithecidae 86205

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

Rhesus monkey: host

Taxa Notes

Animals, Chordates, Mammals, Nonhuman Mammals, Nonhuman Vertebrates,
 Nonhuman Primates, Primates, Vertebrates

ORGN Classifier

Herpesviridae 03115

Super Taxa

dsDNA Viruses; Viruses; Microorganisms

Organism Name

cmv [cytomegalovirus]: pathogen

Taxa Notes

Double-Stranded DNA Viruses, Microorganisms, Viruses

ORGN Classifier

Leporidae 86040

Super Taxa

Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

Dutch belted rabbit: host

Taxa Notes

Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman
 Mammals, Vertebrates

RN 173720-57-5 (GEM 132)

14762-75-5 (CARBON-14)

15117-53-0 (SULFUR-35)

126184-84-7 (14C)

L81 ANSWER 4 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1997:235371 BIOSIS

DN PREV199799534574

TI **Antisense oligonucleotides** inhibit vascular

endothelial growth factor (VEGF) expression in normal human epidermal
 keratinocytes.

AU Smyth, Adrienne P. [Reprint author]; Rook, Susan L.; Detmar, Michael;
 Robinson, Gregory S.

CS **Hybridon Inc., Worcester, MA, USA**

SO Journal of Investigative Dermatology, (1997) Vol. 108, No. 4, pp. 678.

Meeting Info.: **Annual Meeting of the Society for Investigative**
Dermatology. Washington, D.C., USA. April 23-27, 1997.

CODEN: JIDEAE. ISSN: 0022-202X.

DT **Conference; (Meeting)**

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LA English

ED Entered STN: 2 Jun 1997
 Last Updated on STN: 2 Jun 1997

CC **General biology - Symposia, transactions and proceedings 00520**
 Cytology - Human 02508
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Endocrine - General 17002
 Endocrine - Pituitary 17014
 Integumentary system - Physiology and biochemistry 18504
 Integumentary system - Pathology 18506

IT Major Concepts
 Cell Biology; Dermatology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Integumentary System (Chemical Coordination and Homeostasis)

IT Miscellaneous Descriptors
ANTISENSE PHOSPHOROTHIOATE OLIGONUCLEOTIDE
 ; ENDOCRINE SYSTEM; EPIDERMAL KERATINOCYTES; EXPRESSION; INTEGUMENTARY SYSTEM; INTEGUMENTARY SYSTEM DISEASE; MESSENGER RNA; MRNA; PSORIASIS; TRANSFORMING GROWTH FACTOR-ALPHA; VASCULAR ENDOTHELIAL GROWTH FACTOR

ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 human
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L81 ANSWER 5 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1997:197793 BIOSIS
 DN PREV199799496996
 TI Synthesis and evaluation of bioreversible conjugates of
oligonucleoside phosphorothioates.
 AU Ho, Nan-Hui; Yu, Dong; Iyer, Radhakrishnan P.; Agrawal,
 Sudhir
 CS Hybridon Inc., One Innovation Drive, Worcester, MA 01605, USA
 SO Abstracts of Papers American Chemical Society, (1997) Vol. 213,
 No. 1-3, pp. MEDI 119.
 Meeting Info.: 213th National Meeting of the American Chemical
 Society. San Francisco, California, USA. April 13-17, 1997.
 CODEN: ACSRAL. ISSN: 0065-7727.

DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 2 May 1997
 Last Updated on STN: 2 May 1997

CC **General biology - Symposia, transactions and proceedings 00520**
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Pharmacology - General 22002

IT Major Concepts
 Biochemistry and Molecular Biophysics; Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATES

IT Miscellaneous Descriptors
BIOREVERSIBLE OLIGONUCLEOSIDE PHOSPHOROTHIOATES
 CONJUGATES; CHEMISTRY; EVALUATION; PHARMACOLOGY; PRODRUGS; SYNTHESIS

RN 15181-41-6D (PHOSPHOROTHIOATES)

L81 ANSWER 6 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1996:402658 BIOSIS
 DN PREV199699125014
 TI GEM 91, a gag-antisense phosphorothioate: Mechanisms
 of inhibition of HIV replication and attempts to generate HIV resistance

in vitro.

- AU Yamaguchi, K.; Papp, B.; Zhang, D.; Agrawal, S.; Byrn, Randal A.
[Reprint author]
- CS Deaconess Hosp., One Deaconess Road, Boston, MA 02215, USA
- SO ELEVENTH INTERNATIONAL CONFERENCE ON AIDS. (1996) pp. 69.
Eleventh International Conference on AIDS, Vol. One. One world:
One hope.
Publisher: Eleventh International Conference on AIDS, Vancouver,
British Columbia, Canada.
Meeting Info.: Eleventh International Conference on AIDS, Vol. One.
One world: One hope. Vancouver, British Columbia, Canada. July 7-12,
1996.
- DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
- LA English
- ED Entered STN: 3 Sep 1996
Last Updated on STN: 11 Oct 1996
- CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Replication, transcription, translation 10300
In vitro cellular and subcellular studies 32600
Medical and clinical microbiology - Virology 36006
Chemotherapy - Antiviral agents 38506
- IT Major Concepts
Infection; Molecular Genetics (Biochemistry and Molecular Biophysics);
Pharmacology
- IT Chemicals & Biochemicals
PHOSPHOROTHIOATE
- IT Miscellaneous Descriptors
ANTIVIRAL-DRUG; GEM-91; MEETING ABSTRACT; MEETING
POSTER
- ORGN Classifier
Retroviridae 03305
Super Taxa
DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
Organism Name
human immunodeficiency virus
Taxa Notes
DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses
- RN 15181-41-6 (PHOSPHOROTHIOATE)
- L81 ANSWER 7 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
- AN 1996:256504 BIOSIS
- DN PREV199698812633
- TI Dose-dependent pharmacokinetics and metabolism of a hybrid
oligonucleotide phosphorothioate in rats.
- AU Lu, Z. [Reprint author]; Liu, T. [Reprint author]; Habus, I.; Jiang, Z.;
Agrawal, S.; Zhang, R.
- CS Univ. Ala., Birmingham, AL 35294, USA
- SO Proceedings of the American Association for Cancer Research
Annual Meeting, (1996) Vol. 37, No. 0, pp. 352.
Meeting Info.: 87th Annual Meeting of the American Association for
Cancer Research. Washington, D.C., USA. April 20-24, 1996.
ISSN: 0197-016X.
- DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
- LA English
- ED Entered STN: 31 May 1996
Last Updated on STN: 31 May 1996
- CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506

Genetics - Animal 03506
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Pathology - Therapy 12512
 Metabolism - Nucleic acids, purines and pyrimidines 13014
 Pharmacology - Drug metabolism and metabolic stimulators 22003
 Neoplasms - Biochemistry 24006
 Neoplasms - Therapeutic agents and therapy 24008
 Genetics of bacteria and viruses 31500
 Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506
 IT Major Concepts
 Cell Biology; Genetics; Infection; Metabolism; Pharmacology; Tumor
 Biology
 IT Chemicals & Biochemicals
 PHOSPHOROTHIOATE
 IT Miscellaneous Descriptors
 ANTIVIRAL ACTIVITY; **MEETING ABSTRACT**; **MEETING POSTER**
 ; PLASMA CONCENTRATION; URINARY EXCRETION; 2-COMPARTMENT MODEL
 ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates
 ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 human immunodeficiency virus
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses
 RN 15181-41-6 (**PHOSPHOROTHIOATE**)
 L81 ANSWER 8 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1996:256499 BIOSIS
 DN PREV199698812628
 TI Protein kinase A-directed **antisense** restrains tumor growth: Use
 of **phosphorothioate oligonucleotides** containing
 segments of either 2'-O-methyl-oligoribonucleotide or
 methylphosphate oligonucleotide.
 AU Cho-Chung, Y. S. [Reprint author]; Nesterova, M. [Reprint author];
 Agrawal, S.; Noguchi, K.
 CS National Cancer Inst., Bethesda, MD 20892, USA
 SO **Proceedings** of the American Association for Cancer Research
 Annual **Meeting**, (1996) Vol. 37, No. 0, pp. 351.
 Meeting Info.: **87th Annual Meeting of the American Association for**
 Cancer Research. Washington, D.C., USA. April 20-24, 1996.
 ISSN: 0197-016X.
 DT **Conference; (Meeting)**
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)
 LA English
 ED Entered STN: 31 May 1996
 Last Updated on STN: 11 Jul 1996
 CC **General biology - Symposia, transactions and proceedings** 00520
 Cytology - Animal 02506
 Cytology - Human 02508
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Enzymes - Chemical and physical 10806

Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Development and Embryology - Morphogenesis 25508

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Development;
Enzymology (Biochemistry and Molecular Biophysics); Oncology (Human
Medicine, Medical Sciences)

IT Chemicals & Biochemicals
PROTEIN KINASE A; RNASE H

IT Miscellaneous Descriptors
CANCER; DNA; EXPERIMENTAL THERAPEUTICS; **MEETING ABSTRACT**;
MEETING POSTER; PHARMACODYNAMICS; RNA; RNASE H ACTIVATION

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
Rodents, Vertebrates

RN 142008-29-5 (PROTEIN KINASE A)
9050-76-4Q (RNASE H)
63774-49-2Q (RNASE H)

L81 ANSWER 9 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:254013 BIOSIS
DN PREV199698810142
TI Synthesis and biophysical properties of methylphosphotriesters.
AU Devlin, Theresa; Iyer, Radhakrishnan P.; Yu, Dong; Ho, Nan-Hui;
Agrawal, Sudhir
CS Hybridon Inc., One Innovation Drive, Worcester, MA 01605, USA
SO Abstracts of Papers American Chemical Society, (1996) Vol. 211,
No. 1-2, pp. ORGN 358.
Meeting Info.: 211th American Chemical Society National Meeting.
New Orleans, Louisiana, USA. March 24-28, 1996.
CODEN: ACSRAL. ISSN: 0065-7727.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English
ED Entered STN: 31 May 1996
Last Updated on STN: 31 May 1996

CC General biology - Symposia, transactions and proceedings 00520
Genetics - General 03502
Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Diagnostic 12504
Pharmacology - General 22002

IT Major Concepts
Biochemistry and Molecular Biophysics; Genetics; Pharmacology

IT Miscellaneous Descriptors
DIAGNOSTICS; **MEETING ABSTRACT**; **METHYLPHOSPHOTRIESTER**
OLIGONUCLEOTIDE; **PHOSPHOROTHIOATE ANALOG**; **POTENTIAL**

THERAPEUTIC AGENT; SYNTHETIC METHOD

L81 ANSWER 10 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1995:515775 BIOSIS
 DN PREV199598530075
 TI Rats treated with **antisense oligonucleotides** to APP
 and APO-E retain place, cue, and motor memory.
 AU Marotta, C. A. [Reprint author]; Agrawal, S.; Binsack, D. P.
 CS Dep. Psychiatry Human Behavior, Dep. Neurosci., Brown Univ., Providence,
 RI 02192, USA
 SO Society for Neuroscience **Abstracts**, (1995) Vol. 21, No. 1-3, pp.
 1713.
 Meeting Info.: **25th Annual Meeting of the Society for Neuroscience**
 . San Diego, California, USA. November 11-16, 1995.
 ISSN: 0190-5295.
 DT **Conference; (Meeting)**
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)
 LA English
 ED Entered STN: 5 Dec 1995
 Last Updated on STN: 6 Dec 1995
 CC **General biology - Symposia, transactions and proceedings . 00520**
 Behavioral biology - Animal behavior 07003
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Biochemistry studies - Lipids 10066
 Pathology - Therapy 12512
 Nervous system - Physiology and biochemistry 20504
 Nervous system - Pathology 20506
 Psychiatry - Psychopathology, psychodynamics and therapy 21002
 Pharmacology - Neuropharmacology 22024
 IT Major Concepts
 Behavior; Biochemistry and Molecular Biophysics; Nervous System (Neural
 Coordination); Pharmacology
 IT Chemicals & Biochemicals
 AMYLOID
 IT Miscellaneous Descriptors
 ALZHEIMER'S DISEASE; AMYLOID PRECURSOR PROTEIN; **ANTISENSE**
 COMPOUNDS; BEHAVIORAL FUNCTION IMPACT; BETA-AMYLOID; **MEETING**
 ABSTRACT; MEETING POSTER; PHOSPHOROTHIOATE
 OLIGONUCLEOTIDE; THERAPEUTIC POTENTIAL
 ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates
 RN 11061-24-8 (AMYLOID)

L81 ANSWER 11 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1995:239963 BIOSIS
 DN PREV199598254263
 TI Large scale synthesis of **antisense**
oligodeoxyribonucleotide phosphorothioate.
 AU Tang, Jimmy X.; Tang, Jin-Yan
 CS **Hybridon, Inc., One Innovation Drive, Worcester, MA 01605, USA**
 SO **Abstracts of Papers American Chemical Society**, (1995) Vol. 209,
 No. 1-2, pp. MEDI 222.
 Meeting Info.: **209th American Chemical Society National Meeting.**
 Anaheim, California, USA. April 2-6, 1995.

CODEN: ACSRAL. ISSN: 0065-7727.

DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LA English

ED Entered STN: 9 Jun 1995
Last Updated on STN: 11 Jul 1995

CC **General biology - Symposia, transactions and proceedings 00520**
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biophysics - Molecular properties and macromolecules 10506
Pharmacology - General 22002

IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATE

IT Miscellaneous Descriptors
MEETING ABSTRACT; MEETING POSTER; PHARMACEUTICALS;
SYNTHETIC METHOD

RN 15181-41-6 (**PHOSPHOROTHIOATE**)

L81 ANSWER 12 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1995:186634 BIOSIS

DN PREV199598200934

TI Plasma- and serum-protein binding of **antisense oligodeoxynucleotide phosphorothioates** in experimental animals and humans.

AU Zhang, X. [Reprint author]; Lu, Z. [Reprint author]; Diasio, R. B. [Reprint author]; Jiang, Z.; Tan, W.; Agrawal, S.; Zhang, R. [Reprint author]

CS Dep. Pharmacol. Toxicol., Univ. Ala., Birmingham, AL 35294, USA

SO **Proceedings of the American Association for Cancer Research Annual Meeting, (1995) Vol. 36, No. 0, pp. 411.**
Meeting Info.: Eighty-sixth Annual Meeting of the American Association for Cancer Research. Toronto, Ontario, Canada. March 18-22, 1995.
ISSN: 0197-016X.

DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 5 May 1995
Last Updated on STN: 15 May 1995

CC **General biology - Symposia, transactions and proceedings 00520**
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - Virology 36006
Chemotherapy - Antiviral agents 38506

IT Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Infection; Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATES

IT Miscellaneous Descriptors
ACQUIRED IMMUNODEFICIENCY SYNDROME THERAPY; MEETING ABSTRACT;
MESSENGER RNA

ORGN Classifier
Caviidae 86300
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
guinea-pig

Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates

ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Hominidae
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
 Leporidae 86040
 Super Taxa
 Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 rabbit
 Taxa Notes
 Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman
 Mammals, Vertebrates

ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 rat
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates

ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 human immunodeficiency virus
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses

RN 15181-41-6D (PHOSPHOROTHIOATES)

L81 ANSWER 13 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1995:186633 BIOSIS
 DN PREV199598200933
 TI In vivo stability, pharmacokinetics, and metabolism of a "hybrid"
 oligonucleotide phosphorothioate in rats.
 AU Lu, Z. [Reprint author]; Zhao, H. [Reprint author]; Diasio, R. B. [Reprint
 author]; Habus, I.; Jiang, Z.; Agrawal, S.; Zhang, R. [Reprint
 author]
 CS Dep. Pharmacol. Toxicol., Univ. Ala., Birmingham, AL 35294, USA
 SO **Proceedings** of the American Association for Cancer Research
 Annual Meeting, (1995) Vol. 36, No. 0, pp. 411.
 Meeting Info.: **Eighty-sixth Annual Meeting of the American
 Association for Cancer Research.** Toronto, Ontario, Canada. March
 18-22, 1995.
 ISSN: 0197-016X.
 DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 5 May 1995
 Last Updated on STN: 15 May 1995
 CC **General biology - Symposia, transactions and proceedings 00520**
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Metabolism - Nucleic acids, purines and pyrimidines 13014
 Pharmacology - Drug metabolism and metabolic stimulators 22003

Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506

IT Major Concepts
 Infection; Metabolism; Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATE

IT Miscellaneous Descriptors
MEETING ABSTRACT; THERAPEUTIC AGENTS

ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates

ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 human immunodeficiency virus
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses

RN 15181-41-6 (**PHOSPHOROTHIOATE**)

L81 ANSWER 14 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1995:186350 BIOSIS
 DN PREV199598200650
 TI Mathematical modeling of biodistribution of an **antisense oligodeoxynucleotide phosphorothioate**.
 AU Liu, T. [Reprint author]; Lu, Z. [Reprint author]; Diasio, R. B. [Reprint author]; Agrawal, S.; Zhang, R. [Reprint author]
 CS Univ. Alabama, Birmingham, AL 35294, USA
 SO **Proceedings of the American Association for Cancer Research Annual Meeting**, (1995) Vol. 36, No. 0, pp. 364.
 Meeting Info.: **Eighty-sixth Annual Meeting of the American Association for Cancer Research**. Toronto, Ontario, Canada. March 18-22, 1995.
 ISSN: 0197-016X.

DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)

LA English
 ED Entered STN: 5 May 1995
 Last Updated on STN: 15 May 1995

CC **General biology - Symposia, transactions and proceedings 00520**
 Mathematical biology and statistical methods 04500
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biophysics - Molecular properties and macromolecules 10506
 Biophysics - Biocybernetics 10515
 Metabolism - Nucleic acids, purines and pyrimidines 13014
 Blood - Blood and lymph studies 15002
 Pharmacology - Drug metabolism and metabolic stimulators 22003

IT Major Concepts
 Blood and Lymphatics (Transport and Circulation); Mathematical Biology (Computational Biology); Metabolism; Models and Simulations (Computational Biology); Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATE

IT Miscellaneous Descriptors
MEETING ABSTRACT; PHARMACOKINETICS; PLASMA CONCENTRATION; TISSUE CONCENTRATION

ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 rat
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates
 RN 15181-41-6 (PHOSPHOROTHIOATE)

L81 ANSWER 15 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1995:149433 BIOSIS
 DN PREV199598163733
 TI In vivo stability and pharmacokinetics of an anti-HIV **antisense**
 oligonucleotide phosphorothioate (GEM 91) in rats and
 HIV-infected individuals.
 AU Zhang, R. [Reprint author]; Lu, Z. [Reprint author]; Yan, J. [Reprint
 author]; Diasio, R. B. [Reprint author]; Jiang, Z.; Temsamani, J.;
 Schechter, P. J.; Agrawal, S.
 CS Univ. Alabama, Birmingham, AL, USA
 SO AMERICAN SOCIETY FOR MICROBIOLOGY. (1995) pp. 144. Human retroviruses and
 related infections.
 Publisher: American Society for Microbiology (ASM), Books Division, 1325
 Massachusetts Ave. NW, Washington, DC 20005-4171, USA.
 Meeting Info.: **2nd National Conference**. Washington, D.C., USA.
 January 29-February 2, 1995.
 ISBN: 1-55581-097-7.
 DT **Conference; (Meeting)**
 Conference; Abstract; (Meeting Abstract)
 Conference; (Meeting Poster)
 LA English
 ED Entered STN: 3 Apr 1995
 Last Updated on STN: 23 May 1995
 CC **General biology - Symposia, transactions and proceedings 00520**
 Clinical biochemistry - General methods and applications 10006
 Comparative biochemistry 10010
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biophysics - Molecular properties and macromolecules 10506
 Pathology - Therapy 12512
 Metabolism - Nucleic acids, purines and pyrimidines 13014
 Blood - Blood and lymph studies 15002
 Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
 Urinary system - Physiology and biochemistry 15504
 Pharmacology - Drug metabolism and metabolic stimulators 22003
 Pharmacology - Clinical pharmacology 22005
 Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport
 and Circulation); Clinical Chemistry (Allied Medical Sciences);
 Hematology (Human Medicine, Medical Sciences); Infection; Metabolism;
 Pharmacology; Urinary System (Chemical Coordination and Homeostasis)
 IT Chemicals & Biochemicals
 PHOSPHOROTHIOATE
 IT Miscellaneous Descriptors
 ANTIVIRAL-DRUG; BIOSTABILITY; GEM 91; **MEETING ABSTRACT;**
 MEETING POSTER; PLASMA DISAPPEARANCE; URINARY EXCRETION
 ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name

human
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates
 ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates
 ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 human immunodeficiency virus
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses
 RN 15181-41-6 (**PHOSPHOROTHIOATE**)

L81 ANSWER 16 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1994:464513 BIOSIS
 DN PREV199497477513
 TI **Antisense oligonucleotide phosphorothioates**
 inhibit primary HIV-1 isolates in peripheral blood lymphocytes.
 AU Sun, D. [Reprint author]; Weichold, F. F. [Reprint author]; Lusso, P.
 [Reprint author]; Crowley, R. [Reprint author]; **Agrawal, S.**;
 Zamecnik, P.; Gallo, R. C. [Reprint author]; Lisziewicz, J. [Reprint
 author]
 CS Lab. Tumor Cell Biol., NCI, NIH, Bethesda, MD, USA
 SO AIDS Research and Human Retroviruses, (1994) Vol. 10, No. SUPPL. 1, pp.
 S32.
 Meeting Info.: **Annual Meeting of the Laboratory of Tumor Cell**
Biology. Bethesda, Maryland, USA. August 22-28, 1993.
 CODEN: ARHRE7. ISSN: 0889-2229.
 DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 31 Oct 1994
 Last Updated on STN: 1 Nov 1994
 CC **General biology - Symposia, transactions and proceedings 00520**
 Cytology - Human 02508
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Blood - Blood cell studies 15004
 Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
 Genetics of bacteria and viruses 31500
 Immunology - Immunopathology, tissue immunology 34508
 Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506
 IT Major Concepts
 Blood and Lymphatics (Transport and Circulation); Cell Biology;
 Clinical Endocrinology (Human Medicine, Medical Sciences); Genetics;
 Hematology (Human Medicine, Medical Sciences); Infection; Pharmacology
 IT Chemicals & Biochemicals
PHOSPHOROTHIOATES
 IT Miscellaneous Descriptors
 ANTIVIRAL ACTIVITY; **MEETING ABSTRACT**; THERAPEUTIC
 IMPLICATION; VIRAL REPLICATION
 ORGN Classifier
 Hominidae 86215
 Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Hominidae
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates
 ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 human immunodeficiency virus
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses
 RN 15181-41-6D (**PHOSPHOROTHIOATES**)

L81 ANSWER 17 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1994:464512 BIOSIS
 DN PREV199497477512
 TI Inhibition of HIV-1 replication by **antisense oligodeoxynucleotide phosphorothioates** in cultured human macrophages and peripheral blood mononuclear cells.
 AU Weichold, F. F. [Reprint author]; Sun, D. [Reprint author]; Zeman, R. A. [Reprint author]; Agrawal, S.; Zamecmik, P. C.; Gallo, R. C. [Reprint author]; Lisziewicz, J. [Reprint author]
 CS Lab. Tumor Cell Biol., Natl. Cancer Inst., NIH, Bethesda, MD, USA
 SO AIDS Research and Human Retroviruses, (1994) Vol. 10, No. SUPPL. 1, pp. S32.
 Meeting Info.: **Annual Meeting of the Laboratory of Tumor Cell Biology**. Bethesda, Maryland, USA. August 22-28, 1993.
 CODEN: ARHRE7. ISSN: 0889-2229.
 DT **Conference; (Meeting)**
Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 31 Oct 1994
 Last Updated on STN: 1 Nov 1994
 CC **General biology - Symposia, transactions and proceedings 00520**
 Cytology - Human 02508
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Metabolism - General metabolism and metabolic pathways 13002
 Blood - Blood cell studies 15004
 Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
 Blood - Lymphatic tissue and reticuloendothelial system 15008
 Genetics of bacteria and viruses 31500
 Immunology - Immunopathology, tissue immunology 34508
 Medical and clinical microbiology - Virology 36006
 IT Major Concepts
 Blood and Lymphatics (Transport and Circulation); Cell Biology;
 Clinical Endocrinology (Human Medicine, Medical Sciences); Genetics;
 Hematology (Human Medicine, Medical Sciences); Infection; Metabolism
 IT Chemicals & Biochemicals
PHOSPHOROTHIOATES
 IT Miscellaneous Descriptors
 CYTOTOXICITY; GENE EXPRESSION; **MEETING ABSTRACT**; METABOLIC RATE
 ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Hominidae
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates
 ORGN Classifier

Retroviridae 03305

Super Taxa

DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms

Organism Name

human immunodeficiency virus

Taxa Notes

DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses

RN 15181-41-6D (PHOSPHOROTHIOATES)

L81 ANSWER 18 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1994:463439 BIOSIS

DN PREV199497476439

TI The determination of **phosphorothioates** at low concentrations in biological fluids.

AU Ott, Christopher M.; Belenky, Alexei; Bourque, Andre J.; Gemborys, Mark W.; Vilenchik, Maria; Cohen, Aharon S.

CS Hybridon Inc., One Innovatin Drive, Worcester, MA 01605, USA

SO Abstracts of Papers American Chemical Society, (1994) Vol. 208, No. 1-2, pp. ANYL 158.

Meeting Info.: 208th National Meeting of the American Chemical Society. Washington, D.C., USA. August 21-25, 1994.

CODEN: ACSRAL. ISSN: 0065-7727.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 31 Oct 1994

Last Updated on STN: 1 Nov 1994

CC Biochemistry methods - General 10050

Biochemistry studies - General 10060

Biophysics - Methods and techniques 10504

Biophysics - Molecular properties and macromolecules 10506

Metabolism - General metabolism and metabolic pathways 13002

Pharmacology - General 22002

IT Major Concepts

Biochemistry and Molecular Biophysics; Methods and Techniques;

Pharmacology

IT Chemicals & Biochemicals

PHOSPHOROTHIOATES

IT Miscellaneous Descriptors

ANALYTICAL METHOD; DRUG CANDIDATES; GENE EXPRESSION MODULATORS;

MEETING ABSTRACT

RN 15181-41-6D (PHOSPHOROTHIOATES)

L81 ANSWER 19 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 1994:89699 BIOSIS

DN PREV199497102699

TI Genomic pharmacology: Use of **antisense oligonucleotides** to regulate gene expression.

AU Agrawal, Sudhir

CS Hybridon Inc., One Innovation Drive, Worcester, MA 01605, USA

SO Journal of Molecular Recognition, (1993) Vol. 6, No. 1, pp. 9.

Meeting Info.: Tenth International Symposium on Biorecognition and Affinity Technology. Gwatt/Thun, Switzerland. October 1993.

CODEN: JMORE4. ISSN: 0952-3499.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 5 Mar 1994

Last Updated on STN: 5 Mar 1994

CC General biology - Symposia, transactions and proceedings 00520

Genetics - General 03502

Biochemistry studies - Nucleic acids, purines and pyrimidines 10062

Pharmacology - General 22002

IT Major Concepts
 Biochemistry and Molecular Biophysics; Genetics; Pharmacology

IT Miscellaneous Descriptors
 CAPPING; CHIMERA; **MEETING ABSTRACT**; **PHOSPHOROTHIOATE**
 ANALOG; SELF-STABILIZATION

ORGN Classifier
 Organisms 00500
 Super Taxa
 Organisms
 Organism Name
 organisms
 Taxa Notes
 Organisms

L81 ANSWER 20 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1993:424656 BIOSIS
 DN PREV199345072281
 TI High-performance liquid chromatography and capillary gel electrophoresis
 as applied to **antisense** DNA.
 AU Cohen, Aharon S. [Reprint author]; Vilenchik, Maria; Dudley, Judith L.;
 Gemborys, Mark W.; Bourque, Andre J.
 CS **Hybridon Inc., Worcester, MA 01605, USA**
 SO Journal of Chromatography, (1993) Vol. 638, No. 2, pp. 293-301.
 Meeting Info.: **8th International Symposium on Capillary**
Electrophoresis and Isotachophoresis. Rome, Italy. October 6-9, 1992.

DT Article
 Conference; (Meeting)

LA English
 ED Entered STN: 15 Sep 1993
 Last Updated on STN: 15 Sep 1993

CC **General biology - Symposia, transactions and proceedings** 00520
 Genetics - General 03502
 Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
 Biophysics - Methods and techniques 10504

IT Major Concepts
 Biochemistry and Molecular Biophysics; Genetics; Methods and Techniques

IT Chemicals & Biochemicals
PHOSPHOROTHIOATES

IT Miscellaneous Descriptors
 ANALYTICAL METHOD; **PHOSPHOROTHIOATES**

ORGN Classifier
 Organisms 00500
 Super Taxa
 Organisms
 Organism Name
 organisms
 Taxa Notes
 Organisms

RN 15181-41-6D (**PHOSPHOROTHIOATES**)

L81 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1993:333864 BIOSIS
 DN PREV199345028589
 TI 3'-End modified oligodeoxynucleotide phosphorothioates
 : Synthesis, properties and antiviral activity.
 AU Tang, J. Y.; Guo, Q.; Roskey, A.; Agrawal, S.
 CS **Hybridon Inc., One Innovation Dr., Biotechnology Res. Park,**
Worcester, MA 01605, USA
 SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART E,
 pp. 214.
 Meeting Info.: **Keystone Symposium on Genetically Targeted Research**
and Therapeutics: Antisense and Gene Therapy. Keystone, Colorado,
 USA. April 12-18, 1993.

ISSN: 0733-1959.

DT **Conference; (Meeting)**
 LA English
 ED Entered STN: 16 Jul 1993
 Last Updated on STN: 31 Aug 1993
 CC **General biology - Symposia, transactions and proceedings 00520**
 Cytology - General 02502
 Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biophysics - Molecular properties and macromolecules 10506
 Pharmacology - General 22002
 Tissue culture, apparatus, methods and media 32500
 Virology - Animal host viruses 33506
 Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506
 IT Major Concepts
 Cell Biology; Infection; Pharmacology
 IT Chemicals & Biochemicals
 PHOSPHOROTHIOATES
 IT Miscellaneous Descriptors
 ABSTRACT; TISSUE CULTURE
 ORGN Classifier
 Viruses 03000
 Super Taxa
 Microorganisms
 Organism Name
 animal viruses
 Taxa Notes
 Microorganisms, Viruses
 RN 15181-41-6D (**PHOSPHOROTHIOATES**)

L81 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1993:333843 BIOSIS
 DN PREV199345028568
 TI 3' End modified oligodeoxynucleotides phosphorothioate
 : Pharmacokinetics and stability in mice.
 AU Temsamani, J.; Tang, J.-Y.; Padmapriya, A.; Kubert, M.; Agarwal, S.
 CS Hybridon Inc., One Innovation Dr., Biotechnology Research Park,
 Worcester, MA 01605, USA
 SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART E,
 pp. 209.
 Meeting Info.: Keystone Symposium on Genetically Targeted Research
 and Therapeutics: Antisense and Gene Therapy. Keystone, Colorado,
 USA. April 12-18, 1993.
 ISSN: 0733-1959.

DT **Conference; (Meeting)**
 LA English
 ED Entered STN: 16 Jul 1993
 Last Updated on STN: 31 Aug 1993
 CC **General biology - Symposia, transactions and proceedings 00520**
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biophysics - Molecular properties and macromolecules 10506
 Metabolism - Nucleic acids, purines and pyrimidines 13014
 Digestive system - Physiology and biochemistry 14004
 Urinary system - Physiology and biochemistry 15504
 Pharmacology - Drug metabolism and metabolic stimulators 22003
 IT Major Concepts
 Digestive System (Ingestion and Assimilation); Metabolism;
 Pharmacology; Urinary System (Chemical Coordination and Homeostasis)
 IT Chemicals & Biochemicals
 PHOSPHOROTHIOATE
 IT Miscellaneous Descriptors
 ABSTRACT; KIDNEY LEVELS; LIVER

ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates
 RN 15181-41-6 (**PHOSPHOROTHIOATE**)

L81 ANSWER 23 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1993:333783 BIOSIS
 DN PREV199345028508
 TI Cellular uptake and biologic efficacy of **phosphodiester, phosphorothioate, and chimeric oligodeoxynucleotides.**
 AU Krieg, Arthur M. [Reprint author]; Zhao, Qiuyan [Reprint author]; Matson, Sara [Reprint author]; Herrara, Charles J.; Fisher, Eric
 CS Univ. Iowa, Iowa City, IA 52242, USA
 SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART E, pp. 193.
 Meeting Info.: **Keystone Symposium on Genetically Targeted Research and Therapeutics: Antisense and Gene Therapy.** Keystone, Colorado, USA. April 12-18, 1993.
 ISSN: 0733-1959.
 DT **Conference; (Meeting)**
 LA English
 ED Entered STN: 16 Jul 1993
 Last Updated on STN: 31 Aug 1993
 CC Cytology - Animal 02506
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Biophysics - Molecular properties and macromolecules 10506
 Enzymes - Chemical and physical 10806
 Blood - Lymphatic tissue and reticuloendothelial system 15008
 Pharmacology - Immunological processes and allergy 22018
 Immunology - Immunopathology, tissue immunology 34508
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Immune System (Chemical Coordination and Homeostasis); Pharmacology
 IT Chemicals & Biochemicals
 PHOSPHOROTHIOATE; NUCLEASE
 IT Miscellaneous Descriptors
 ABSTRACT; IMMUNOLOGIC-DRUG; IMMUNOSUPPRESSIVE PROTEIN ANTISENSE SEQUENCE; LYMPHOCYTE REACTIVATION; METHYLPHOSPHONATE OLIGONUCLEOTIDES; NUCLEASE RESISTANCE; PHOSPHOROTHIOATE OLIGONUCLEOTIDES

ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 mouse
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates
 RN 15181-41-6 (**PHOSPHOROTHIOATE**)
 9026-81-7 (**NUCLEASE**)

L81 ANSWER 24 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1993:333769 BIOSIS
 DN PREV199345028494

TI Self-stabilized antisense oligonucleotide
phosphorothioates: Synthesis, properties and anti-viral activity.
AU Agrawal, Sudhir [Reprint author]; Tang, Jin Yan
CS Hybridon Inc., One Innovation Dr., Worcester, MA 01605, USA
SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART E,
pp. 189.
Meeting Info.: Keystone Symposium on Genetically Targeted Research
and Therapeutics: Antisense and Gene Therapy. Keystone, Colorado,
USA. April 12-18, 1993.
ISSN: 0733-1959.

DT Conference; (Meeting)
LA English
ED Entered STN: 16 Jul 1993
Last Updated on STN: 31 Aug 1993

CC General biology - Symposia, transactions and proceedings 00520
Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biophysics - Molecular properties and macromolecules 10506
Pharmacology - General 22002
Virology - Animal host viruses 33506
Chemotherapy - Antiviral agents 38506

IT Major Concepts
Biochemistry and Molecular Biophysics; Microbiology; Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATES

IT Miscellaneous Descriptors
ABSTRACT; ANTIVIRAL AGENT; HAIRPIN LOOP STRUCTURE; SYNTHETIC
METHOD

RN 15181-41-6D (PHOSPHOROTHIOATES)

L81 ANSWER 25 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1993:155421 BIOSIS
DN PREV199344074221

TI Capped oligodeoxynucleotide phosphorothioates:
Pharmacokinetics and stability in mice.

AU Temsamani, J. [Reprint author]; Tang, J.-Y. [Reprint author];
Agrawal, Sudhir

CS Hybridon Inc., One Innovation Drive, Worcester, MA 01605, USA
SO Baserga, R. [Editor]; Denhardt, D. T. [Editor]. Ann. N. Y. Acad. Sci.,
(1992) pp. 318-320. Annals of the New York Academy of Sciences; Antisense
strategies.
Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, New
York 10021, USA. Series: Annals of the New York Academy of Sciences.
Meeting Info.: Conference. Philadelphia, Pennsylvania, USA.
January 12-15, 1992.
CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 0-89766-748-4 (paper), 0-89766-747-6
(cloth).

DT Article
Conference; (Meeting)
LA English
ED Entered STN: 19 Mar 1993
Last Updated on STN: 16 May 1993

CC Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biophysics - Molecular properties and macromolecules 10506
Pathology - Therapy 12512
Metabolism - Nucleic acids, purines and pyrimidines 13014
Blood - Blood and lymph studies 15002
Pharmacology - Drug metabolism and metabolic stimulators 22003
Genetics of bacteria and viruses 31500
Virology - Animal host viruses 33506
Medical and clinical microbiology - Virology 36006
Chemotherapy - Antiviral agents 38506

IT Major Concepts
 Biochemistry and Molecular Biophysics; Metabolism; Microbiology;
 Pharmacology

IT Chemicals & Biochemicals
PHOSPHOROTHIOATES

IT Miscellaneous Descriptors
 ANTI-HUMAN IMMUNODEFICIENCY VIRUS TYPE 1; ANTIVIRAL- DRUG;
 BIOAVAILABILITY; MONKEY PLASMA STABILITY; SYNTHETIC METHOD

ORGN Classifier
 Muridae 86375
 Super Taxa
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Muridae
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Rodents, Vertebrates

ORGN Classifier
 Primates 86190
 Super Taxa
 Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Primates
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Mammals, Nonhuman Vertebrates,
 Nonhuman Primates, Primates, Vertebrates

ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 Retroviridae
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses

RN 15181-41-6D (**PHOSPHOROTHIOATES**)

L81 ANSWER 26 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1993:155374 BIOSIS
 DN PREV199344074174
 TI Synthesis and anti-HIV activity of oligoribonucleotides and
 their phosphorothioate analogs.

AU Agrawal, Sudhir [Reprint author]; Tang, J. Y.; Sun, D.; Sarin,
 P. S.; Zamecnik, P. C.

CS Worcester Found. Experimental Biol., 222 Maple Ave., Shrewsbury, MA 01545,
 USA

SO Baserga, R. [Editor]; Denhardt, D. T. [Editor]. Ann. N. Y. Acad. Sci.,
 (1992) pp. 2-10. Annals of the New York Academy of Sciences; Antisense
 strategies.
 Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, New
 York 10021, USA. Series: Annals of the New York Academy of Sciences.
 Meeting Info.: Conference. Philadelphia, Pennsylvania, USA.
 January 12-15, 1992.
 CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 0-89766-748-4 (paper), 0-89766-747-6
 (cloth).

DT Article
Conference; (Meeting)

LA English

ED Entered STN: 19 Mar 1993
 Last Updated on STN: 19 Mar 1993

CC General biology - Symposia, transactions and proceedings 00520
 Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Replication, transcription, translation 10300

Pathology - Therapy 12512
 Pharmacology - Drug metabolism and metabolic stimulators 22003
 Genetics of bacteria and viruses 31500
 Virology - Animal host viruses 33506
 Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506

IT Major Concepts
 Biochemistry and Molecular Biophysics; Genetics; Microbiology;
 Molecular Genetics (Biochemistry and Molecular Biophysics);
 Pharmacology

IT Miscellaneous Descriptors
 GENE THERAPY; SYNTHETIC METHOD; TAT GENE SPLICE ACCEPTOR SITE

ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Organism Name
 human immunodeficiency virus type 1
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses

L81 ANSWER 27 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1990:461417 BIOSIS
 DN PREV199039096778; BR39:96778
 TI INHIBITION OF HIV-1 IN EARLY INFECTED AND CHRONICALLY INFECTED CELLS BY
 ANTISENSE OLIGODEOXYNUCLEOTIDES AND THEIR
 PHOSPHOROTHIOATE ANALOGUES.

AU **AGRAWAL S** [Reprint author]; SUN D; SARIN P; ZAMECNIK P C
 CS WORCESTER FOUNDATION EXP BIOL, MAPLE AVENUE, SHREWSBURY, MASS 01545, USA
 SO Journal of Cellular Biochemistry Supplement, (1990) No. 14 PART D, pp.
 145.
 Meeting Info.: **SYMPOSIUM ON HIV AND AIDS: PATHOGENESIS, THERAPY AND**
 VACCINE HELD AT THE 19TH ANNUAL UCLA (UNIVERSITY OF CALIFORNIA-LOS
 ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, KEYSTONE, COLORADO,
 USA, MARCH 31-APRIL 6, 1990. J CELL BIOCHEM SUPPL.
 ISSN: 0733-1959.

DT **Conference; (Meeting)**
 FS BR
 LA ENGLISH
 ED Entered STN: 13 Oct 1990
 Last Updated on STN: 13 Oct 1990

CC **General biology - Symposia, transactions and proceedings 00520**
 Cytology - Animal 02506
 Biochemistry methods - Nucleic acids, purines and pyrimidines 10052
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Pharmacology - General 22002
 Tissue culture, apparatus, methods and media 32500
 Virology - Animal host viruses 33506
 Chemotherapy - Antiviral agents 38506

IT Major Concepts
 Biochemistry and Molecular Biophysics; Microbiology; Pharmacology

IT Miscellaneous Descriptors
 ABSTRACT HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 ANTIVIRAL AGENT
 MOLT 3 CELL

ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses

L81 ANSWER 28 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1989:484401 BIOSIS

DN PREV198937105520; BR37:105520
 TI **PHOSPHORAMIDATE PHOSPHOROTHIOATE AND
 METHYLPHOSPHONATE ANALOGS OF OLIGODEOXYNUCLEOTIDE
 INHIBITORS OF REPLICATION OF HUMAN IMMUNODEFICIENCY VIRUS.**
 AU **AGRAWAL S** [Reprint author]; GOODCHILD J; CIVEIRA M; SARIN P S;
 ZAMECNIK P C
 CS WORCESTER FOUND EXP BIOL, MAPLE AVE, SHREWSBURY, MA 01545, USA
 SO Nucleosides and Nucleotides, (1989) Vol. 8, No. 5-6, pp. 819-824.
 Meeting Info.: 8TH INTERNATIONAL ROUND TABLE ON NUCLEOSIDES, NUCLEOTIDES,
 AND THEIR BIOLOGICAL APPLICATIONS, ORANGE BEACH, ALABAMA, USA, OCTOBER
 2-5, 1988. NUCLEOSIDES NUCLEOTIDES.
 CODEN: NUNUD5. ISSN: 0732-8311.
 DT **Conference; (Meeting)**
 FS BR
 LA ENGLISH
 ED Entered STN: 26 Oct 1989
 Last Updated on STN: 5 Dec 1989
 CC **General biology - Symposia, transactions and proceedings 00520**
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Replication, transcription, translation 10300
 Metabolism - Nucleic acids, purines and pyrimidines 13014
 Pharmacology - General 22002
 Genetics of bacteria and viruses 31500
 Virology - Animal host viruses 33506
 Immunology - Immunopathology, tissue immunology 34508
 Medical and clinical microbiology - Virology 36006
 Chemotherapy - Antiviral agents 38506
 IT Major Concepts
 Genetics; Immune System (Chemical Coordination and Homeostasis);
 Infection; Metabolism; Microbiology; Molecular Genetics (Biochemistry
 and Molecular Biophysics); Pharmacology
 IT Miscellaneous Descriptors
 ANTIVIRAL-DRUG
 ORGN Classifier
 Retroviridae 03305
 Super Taxa
 DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
 Taxa Notes
 DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses
 RN 22638-09-1Q (**PHOSPHORAMIDATE**)
 41744-81-4Q (**PHOSPHORAMIDATE**)
 15181-41-6 (**PHOSPHOROTHIOATE**)

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 E AGRAWAL S/AU
 L3 388 S E3-E15
 E AGRAWAL SUDHIR/AU
 L4 355 S E3
 E YU D/AU
 L5 440 S E3-E30
 E YU DONG/AU
 L6 449 S E3-E73
 E ZHAO Q/AU
 L7 417 S E3-E17

L8 E ZHAO QUI/AU
1 S E13
E HYBRIDON/PA,CS
L9 346 S E3-E34
SEL RN L1

FILE 'REGISTRY' ENTERED AT 05:58:33 ON 29 JUN 2004

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L12 1 S L10 AND S/ELS
L13 1 S L10 AND P/ELS
L14 2 S L12,L13
L15 STR
L16 50 S L15
L17 1004 S L15 FUL
SAV L17 TEMP LE965/A
L18 STR L15
L19 STR L18
L20 27 S L19 SAM SUB=L17
L21 520 S L19 FUL SUB=L17
SAV L21 LE965A/A
L22 STR L19
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L24 247 S L22 FUL SUB=L21
SAV L24 LE965B/A
L25 4 S L24 AND 5/NR
L26 1 S L25 AND C19H26N8O11P2S2

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L29 1 S L25
L30 1 S L28,L29

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L31 2 S L26
L32 2 S L25
L33 2 S L31,L32
L34 56 S L24
L35 1 S L34 AND L1-L9
E ZHAO QIU/AU
L36 4 S E3
L37 37 S E34
L38 1 S L34 AND L36,L37
L39 1 S L35,L38
L40 3 S L33,L39
L41 279 S L17
L42 13 S L41 AND L1-L9,L36,L37
SEL HIT RN

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L43 24 S E1-E24

FILE 'HCAPLUS' ENTERED AT 06:17:04 ON 29 JUN 2004

L44 3 S L1-L9,L36,L37 AND ?PHOSPHORTHIO?
L45 0 S L1-L9,L36,L37 AND ?PHOSPHOTHIO?
L46 259 S L1-L9,L36,L37 AND ?PHOSPH?(L)?THIO?
L47 256 S L46 AND (?NUCLEO? OR ?NUCLEI?)
E PHOSPHORTHIOATE/CT
E PHOSPHOROTHIOATE/CT
L48 2068 S E5+OLD,NT,PFT OR E6+OLD,NT,PFT OR E7

L49 E E5+ALL
 948 S E28,E27+NT
 E E26+ALL
 L50 2068 S E10,E9+NT
 L51 112 S L46 AND L48-L50
 L52 112 S L47 AND L51
 L53 112 S L51,L52
 L54 99 S L53 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
 L55 112 S L53,L54 AND L48-L50
 L56 115 S L1,L55
 L57 126 S L42,L56
 L58 125 S L57 NOT L40

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FILE 'HCAPLUS' ENTERED AT 06:25:48 ON 29 JUN 2004

FILE 'BIOSIS' ENTERED AT 06:27:41 ON 29 JUN 2004

L59 E KANDIMALLA E/AU
 60 S E3-E8
 E ZHAO Q/AU
 L60 238 S E3-E18
 L61 27 S E103,E104
 E ZHAO QUI/AU
 L62 1 S E7
 E YU D/AU
 L63 760 S E3-E32
 E YU DONG/AU
 L64 154 S E3-E31
 E AGRAWAL S/AU
 L65 573 S E3-E16
 E AGRAWAL SUDHIR/AU
 L66 216 S E3,E4,E5
 E HYBRIDON/PA,CS
 L67 293 S E3-E55
 L68 1979 S L59-L67
 L69 164 S L68 AND (?PHOSPHOROTHIO? OR ?PHOSPHORTHIO? OR ?PHOSPH?(L)?THI
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 SEL DN AN 7 9 10
 L72 3 S L71 AND E1-E6
 L73 26 S L70 NOT L71
 SEL DN AN 26
 L74 25 S L73 NOT E7-E9
 L75 28 S L72,L74
 L76 28 S L75 AND L59-L75
 L77 25 S L76 AND (?OLIGO? OR ?NUCLEI? OR ?NUCLEO?)
 L78 18 S L76 AND ANTISENS?
 L79 27 S L77,L78
 L80 1 S L76 NOT L79
 L81 28 S L79,L80

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